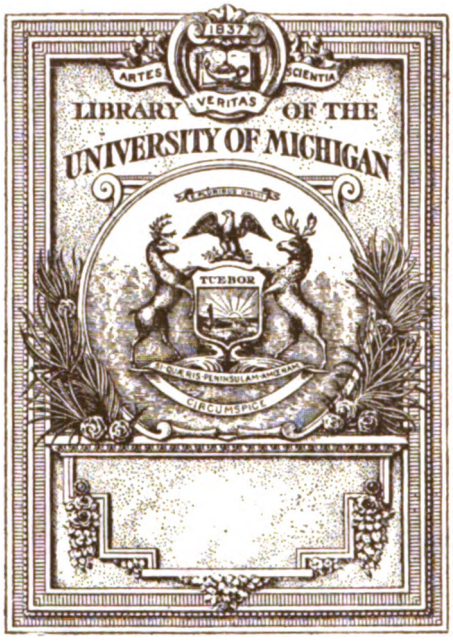

Journal

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Original Communications.

ANOXÆMIA AS A FACTOR IN ACUTE GAS POISONING.

BY JOSEPH BARCROFT, C.B.E., F.R.S.

ANOXÆMIA comprises all those conditions in which the tissues of the body are starved, or partially starved, of oxygen. By derivation the term indicates a deficiency of oxygen in the blood; actually, however, it has come to mean more than this and includes not only conditions in which the tissues lack oxygen because the blood lacks oxygen, but also those in which oxygen-hunger is forced upon the various organs because the quantity of blood passing to them is too small.

Let me, therefore, at the outset, be perfectly definite about what is meant by the term, and about the classification into which the various forms of anoxæmia fall.

In order to be perfectly definite as to where we commence, let me say a few more words about anoxæmia itself before passing to the consideration of its relation to gas poisoning.

Anoxæmia ordinarily is divisible into three classes or main types:—

(1) That in which the pressure of oxygen in the blood is too low. This is known as the *anoxic* type—there is sufficient blood, there is sufficient hæmoglobin in the blood, but the hæmoglobin is in part reduced—the blood in the arteries presents the general appearance of venous blood, and just in so far as it is venous the condition is one of anoxic anoxæmia.

(2) That in which there is too little hæmoglobin in the blood. The pressure of oxygen is normal, the functioning hæmoglobin is saturated with oxygen and is bright red like that of normal arterial blood, the volume of blood which circulates is adequate, but each cubic centimetre of blood contains a deficient quantity of functioning hæmoglobin. This second type of anoxæmia may be called the anæmic type. Examples of it will at once occur to you; ordinary anæmia is the most obvious.

In it the hæmoglobin simply is not there ; but other less evident varieties exist—conditions in which the hæmoglobin present is prevented from functioning, being turned into some kind of pigment other than the respiratory one. It may be converted, for instance, in part into the brown material, methæmoglobin, met with in certain forms of dysentery or in some industrial diseases ; or it may be converted into carboxyhæmoglobin, as in cases of poisoning with mine gas, but in any case it is not present as a functional oxygen carrier.

(3) The anoxæmia may be of the stagnant type, to which I have already alluded, and in which the blood quantity is normal enough, but is delivered to the tissues in insufficient quantity, and therefore the amount of oxygen which reaches them per minute is too small.

What I have said so far may be summarized in the following scheme :—

ANOXÆMIA.

(1) Anoxic Type.	(2) Anæmic Type.	(3) Stagnant Type.
The oxygen pressure is too low.	The quantity of functional hæmoglobin is too small.	The blood is normal, but is supplied to the tissues in insufficient quantities.
The hæmoglobin is not saturated to the normal extent.	The oxygen pressure is normal.	
The blood is dark.	The blood may be normal in colour.	

Having made these preliminary remarks, let me now say that within my knowledge there is no single condition which so aptly illustrates the various types of anoxæmia, and their possible combinations with one another, as does poisoning with pulmonary irritant gases, such as chlorine or phosgene.

My object will be to take you through a number of cases of gas poisoning in which the facts with regard to the blood are known, to point out the type and the degree of anoxæmia which exists in each, and to say what I can not only about anoxæmia itself, but also about the degree to which it is likely to prejudice efficiency of the sufferer, and about the logical indications for treatment.

I allude to the sufferer as "him," but I should make it clear that the cases about which I am going to speak in the first instance were not human beings but goats. Because they were goats, and because goats do not resent having samples of blood withdrawn by the method of intracardiac puncture, it was possible for my staff at the Royal Engineers Station at Porton to follow the changes which took place in normal and gassed goats from day to day, or even from hour to hour.

The goat was gassed by being placed in a respiration chamber, the atmosphere of which contained a standard dose of—usually phosgene—for a given time. He was then kept under observation in the hospital; when samples of blood were required he was laid on his side, the needle of a hypodermic syringe was thrust directly through the body wall and into either ventricle of the heart at will, and the arterial or venous blood withdrawn as required.

Firstly, let me speak to you about the blood of a normal goat. Fig. 1 illustrates the points which I wish to bring out. The scale on the left-hand side is numbered from 0 at the bottom to 100 at the top. It has reference to the quantity of oxygen in the blood. When the corpuscles are fully charged, as they would be if the blood was shed and shaken with oxygen, the blood is said to be saturated and the quantity present in a cubic centimetre is called 100. If the blood is not fully saturated, and it never is in the body, the quantity of oxygen in it is expressed as a percentage. Vertically, then, is measured the quantity of oxygen and horizontally the time in hours, starting from the first observation. What then does the figure show? The top edge of the black area is the oxygen in the arterial blood. If you follow it you will see that there are fluctuations; for instance, seventeen hours after the commencement of this experiment there is more oxygen in the blood than twenty-four hours from

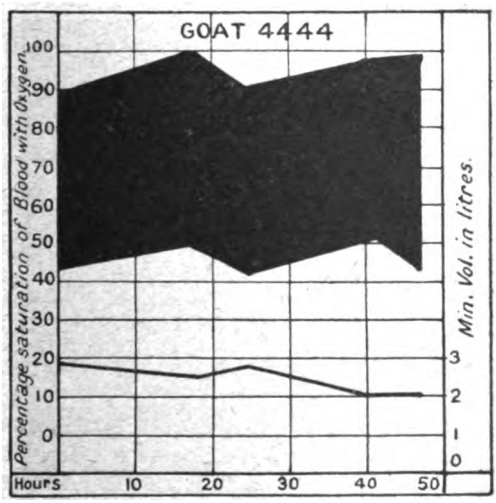

Fig. 1.

zero. These fluctuations however are confined within rather small limits, for the oxygen does not drop below ninety per cent of the full load, nor does it rise above 100 per cent. And the slide is in this respect typical, for out of over sixty determinations which were made on normal goats the great majority showed a saturation of between ninety-four and ninety-eight per cent. The series gave evidence that anything under ninety per cent was to be viewed with suspicion. The lower edge of the black area in a similar way marks the quantity of oxygen in the venous blood. In this particular experiment the quantity of oxygen in the venous blood is as nearly as possible the half of the amount present in the arterial. Returning then to the oxygen in the arterial blood we may say that if it is between ninety and 100 per cent there is no anoxæmia of the anoxic type.

Let me pass to a case of gas poisoning. Goat 2014 (fig. 2) was a mild phosgene case. I introduce it here for the purpose of making clear at the start that gas poisoning does not necessarily involve anoxæmia. Though the oxygen in his arterial blood was dropping gradually as the hours passed and as the case developed, yet there was no evidence that it ever dropped below ninety per cent—the lowest limit which we have set to normality. How then, in a human case, are you to know whether the anoxic type of anoxæmia is present or not? This is a very practical question. It was one which arose in the very early days of gas poisoning. As early as May, 1915, that question had to be settled within my experience in Boulogne, and no doubt in many another place. The answer for practical purposes is simple. If there is cyanosis, there is anoxæmia; if not, anoxæmia, or at all events of the anoxic type, may be ruled out. Cyanosis is not always of the

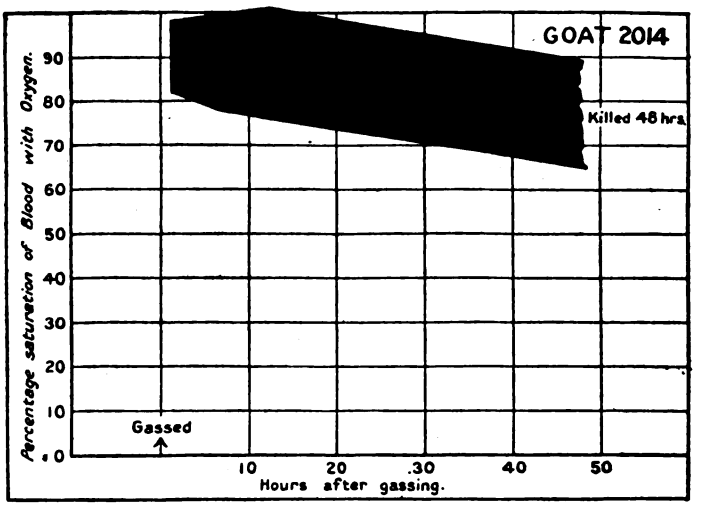

FIG. 2.

same kind; on that point I shall have to speak later, but unless a case shows some kind of cyanosis, oxygen is wasted on it. The matter is perhaps more pertinent than at first sight appears. In a civil case oxygen might be given on the ground that at least it could do no harm. But in war, so much resolves itself into a question of transport, does it not? I think I am not saying anything either untrue or indiscreet if I say that after any large attack with a pulmonary irritant gas, the quantity of oxygen available was never anything like sufficient to supply the needs of the patients for whom it was urgently necessary. To use it on those for whom it was unnecessary was therefore to be avoided for two reasons; to do so involved the withholding of oxygen from some one who required this gas, and also the use of transport which was urgently wanted for other purposes. Economy is an urgent question in the use of oxygen as a therapeutic agent in war.

Let me now pass to another case, goat 2403 (fig. 3). In this goat the oxygen in the arterial blood dropped within the first three hours of gassing to 80 per cent and remained between 80 and 85 per cent until at the end of twenty-seven hours this goat was killed. Clearly we have here a case of anoxic anoxæmia, not fatal within the first day at all events. The question naturally arises "How far is such a degree of anoxæmia harmful?" At this point we are met with one of the disadvantages of working on goats. You cannot tell when a goat has a headache. You can kill it and examine the lungs, you can take blood from its heart or vessels and examine the deficiency of oxygen but you cannot get at its more subjective troubles. But if the goat fails us at this point I can fill in a little of the gap from my own personal experience. I have known what it

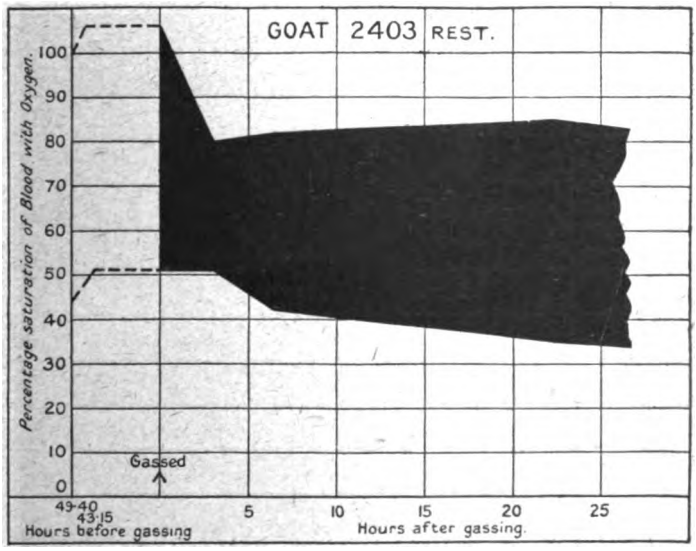

FIG. 3.

was to have the oxygen in my own arterial blood reduced below eighty-five per cent and kept at that level for some time. Sleep was of the lightest and most intermittent character. Headache was acute, vision was impaired and physical work of any considerable amount was out of the question. There is no fight, no possibility of fight in a man whose blood has been reduced suddenly to a saturation with oxygen of eighty-five per cent for twenty-four hours. Nor is there any fight in a goat under the same condition. There is this difference however between the goat and the man. The man may try to fight and herein lies his real danger; the goat will not do so. It is almost impossible to make the anoxæmic goat take any exercise whatever. The particular animal in question No. 2403 did so on one occasion with the result that

we obtained a particularly interesting observation (fig. 4). When he kicked about a little, the oxygen in his arterial blood which had been about eighty-three per cent suddenly dropped to forty-four per cent, the arterial blood became as black as ordinary venous blood. Such a condition if it lasts for any length of time is fatal. Exercise kills the anoxæmic animal as it kills the anoxæmic man. To give a single instance: I have seen an anoxæmic rabbit which was apparently happy in a basket about eighteen inches high; for some reason he jumped over the edge of the basket, only to drop and expire as the result of the effort.

Quite similar occurrences have taken place in gas warfare. Among the earliest instances of phosgene poisoning to which my attention was called

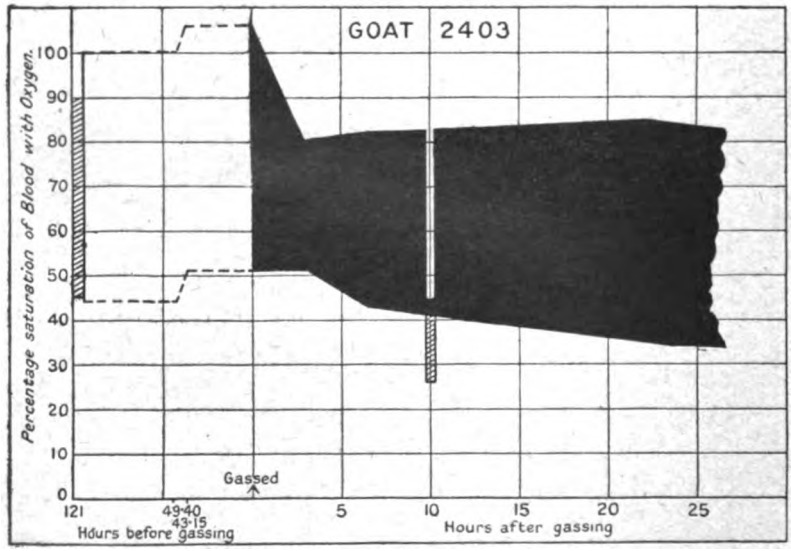

FIG. 4.

were some of this character. The following note kindly given me by Colonel Cummins, C.B., C.M.G., describes a typical one:—

"An officer very slightly gassed was sent to an aid post for examination and was thought, and thought himself, to be quite recovered. He started back to the line and came under shell fire *en route*. He ran to take shelter in a better place just ahead. He got there, sat down in shelter and rapidly died."

It is worth while to linger a moment over these fatal cases in order to inquire what sort of death they died. Did they die of heart failure or of respiratory failure? I think the most truthful thing to say is that they died of brain failure—brain failure which primarily affected the respiration and which involved a certain cardiac element. Let me try to place these respiratory and cardiac factors. When a cat is given an atmosphere to

breathe which contains too little oxygen but is in other respects normal, it passes away very quietly; there are none of the convulsive effects of ordinary asphyxia. Yesterday I saw such a death, the animal was breathing an atmosphere of five per cent oxygen and ninety-five per cent nitrogen. In about five minutes it ceased to breathe, nothing attracted attention, the cat was lying on its side and it simply went out. The heart was beating strongly, and continued to beat for a long time after respiration ceased, the muscles were capable of contraction and it was clear that the respiratory centre in the brain had gradually been losing its rhythmic power and had finally ceased to function. Such is the death from anoxic anoxæmia uncomplicated by exercise. But when exercise is taken and when the oxygen pressure in the arterial blood suffers such a sudden drop

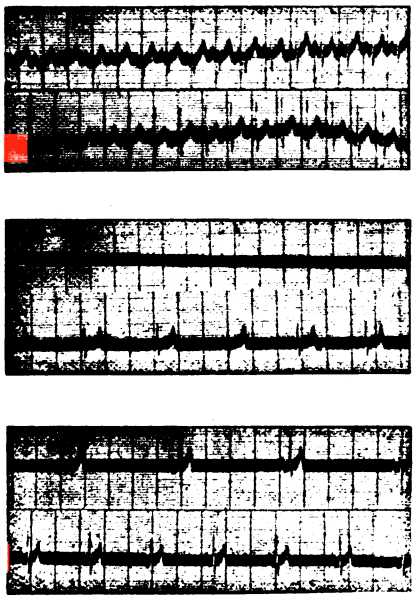

FIG. 5.

as is shown in goat 2403, there is added to the increasing impotence of the respiratory centre another medullary effect, namely, an element of vagus stimulation of the heart. The heart suddenly stops, or rather it is stopped; for the time being the blood flow to the brain is cut down and therefore, added to the suddenly heightened anoxic anoxæmia, there is an extreme form of stagnant anoxæmia. It is probably this introduction of cardiac-vagal element which causes the suddenness of the death.

You may trace the facts which I have put before you in the following slides:—

On fig. 5 there are six tracings, taken from the same rabbit, by Dr. Thomas Lewis. They were taken the day after the rabbit was gassed.

The first two were taken when the animal was at rest. The upright vertical lines correspond to time intervals of $\frac{1}{5}$ of seconds; each complete set of oscillations on the tracing corresponds to one heart-beat. The heart was therefore seen to be beating regularly at the rate of about 280 per minute. The rabbit at a certain juncture struggled violently and died in just the manner which I have described. At the end of the struggling period a record was taken, the third on the figure, the whole record does not contain a single heart-beat. Yet this is but a mere inhibition, for as soon as the animal was really dead, in the sense of having breathed its last, the heart went on again and you may see records taken of the beating heart in the three subsequent tracings. The fourth record in the order was taken immediately after number three, the fifth and sixth about two minutes later.

There is another way in which exercise in the gassed animal may lead to anoxæmia of the stagnant type—the type caused by insufficiency of the circulation. As was shown many years ago by Leonard Hill, when an animal which has been lying down is suddenly made to assume the upright position, with its head upwards and its feet downwards, the arterial pressure as judged by a tracing taken from the carotid artery suffers an initial drop, but very soon re-establishes itself at the old level. The blood impact tends to leave the head momentarily, but only momentarily. In the gassed rabbit the power of the vasomotor system to compensate for changes in posture is much impaired, so that if the animal which has been in the horizontal position is placed suddenly with its head up, the arterial pressure will not only sink, but will remain at a low level. In other words, the circulation through the brain will fail and anoxæmia of the stagnant type will supervene.

To sum up the rôle of anoxæmia as a factor in causing sudden deaths due to exercise :—

EXERCISE CAUSES INCREASED ANOXÆMIA IN GASSED PATIENTS.

Anoxic Type.	Anæmic Type.	Stagnant Type
(*a*) The demand for oxygen by the body is increased but the lung owing to its decreased permeability cannot let it into the blood at the required rate.	Nil	(*a*) Cardio inhibition
(*b*) The vessels in the lung probably dilate in the solid or semi-solid areas and pass blood which does not get oxidized.		(*b*) Lack of vasomotor tone

I have gone somewhat fully into the question of sudden deaths caused by exercise within twenty-four hours of gas poisoning, because the soldier, unlike the goat, will exert himself if he is told to do so; and therefore it becomes the business of those in whose hands his life is to see that no

unnecessary exercise, and most especially no sudden exercise, should be undertaken so long as the soldier is a case of gas poisoning.

After this digression let me return to the consideration of my series of pictures which depict the quantity of oxygen in the blood of gassed goats.

I had chosen goat 2403 because it was a peculiarly uncomplicated case of the anoxic type. The oxygen in the arterial blood rapidly fell to between eighty and eighty-five per cent. That in the venous blood did not fall much below its normal value. In contrast to this figure is one of goat 2952 (fig. 6). The interest in this particular goat to me is that he

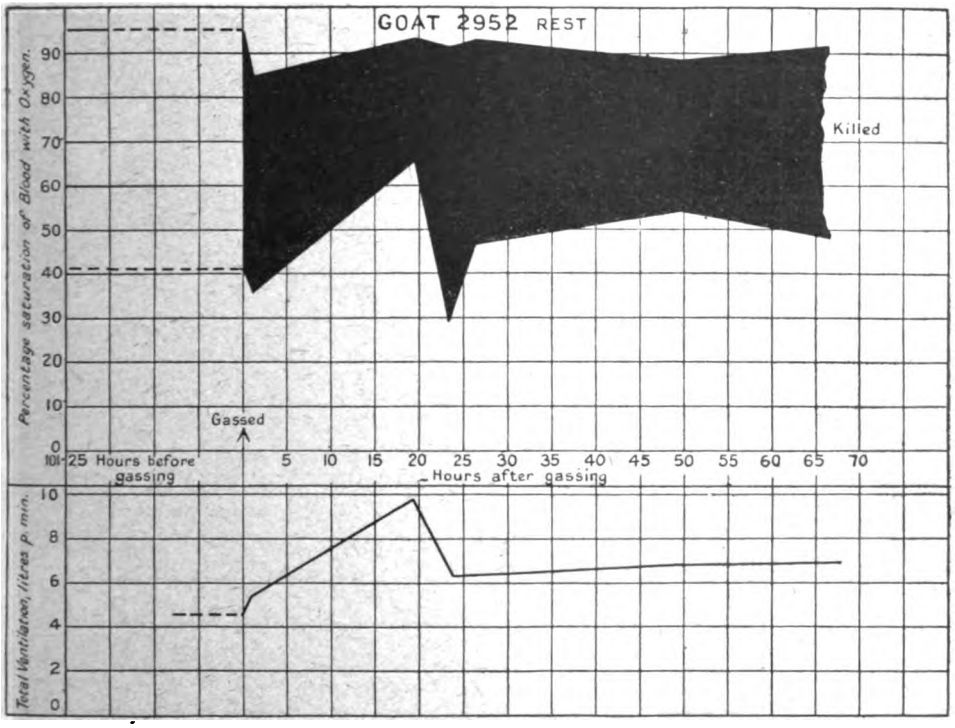

FIG. 6.

fought the anoxæmia successfully; we followed it for sixty-five hours from gassing, and at the end killed him for the purpose of examining his lung, but with the assurance that the goat had overcome.

I shall endeavour to give you some idea of this fight, showing how the units, one by one, which the body has at its disposal were brought into action, and the degree of success which they met.

The First Twenty Hours.—Two hours from zero anoxic anoxæmia had set in.

Unit (*a*).—The respiratory system met this by an increase of the total ventilation. An observation taken seventeen hours after gassing showed

that the amount of air which passed into and out of the respiratory system per minute was just double what it had previously been. This extra ventilation, no doubt, raised the pressure of oxygen in the lungs, and this ended to, and in this case actually did, reduce or stave off the anoxic type of anoxæmia.

Unit (b): The Heart.—All this time a curious thing had been happening to the venous blood (fig. 7) (note the lower edge of the upper black area). The venous blood had been getting redder and redder, so that, normally having a percentage saturation of oxygen of

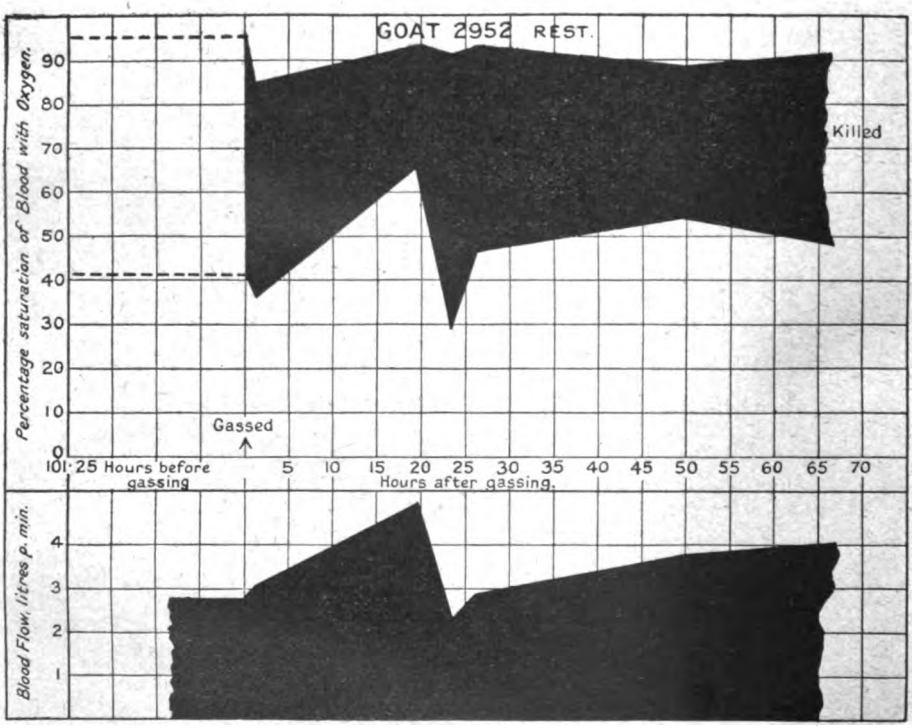

FIG. 7.

40 (which fell shortly after gassing to 36), the oxygen rose from this point, until at the end of nineteen hours it had reached 65. What was the meaning of this rise in the oxygen of the venous blood—or, to put the matter another way, why was only half the normal amount of oxygen leaving the venous blood? It was not that the animal was using less oxygen—in fact he was using a little more [477 cubic centimetres per kilo per hour instead of 408]. There is only one other possibility, then, namely, that the blood was being propelled round the body at double the original rate. Our measurements showed that to be so. The normal volume of blood which traversed the lungs per minute was 2·8 litres;

nineteen hours after gassing, this had risen to 4·9, an amount equal to what passed round the circulation as the result of quite considerable exercise normally. Such, then, was the strain thrown upon the heart. How long could this condition of stress last? How long could the heart and respiratory system function as though the animal was in active exercise when in reality he was impotent to the last degree with gas poisoning?

The Twentieth to the Twenty-fifth Hour.—The change came between the nineteenth to twenty-fourth hours.

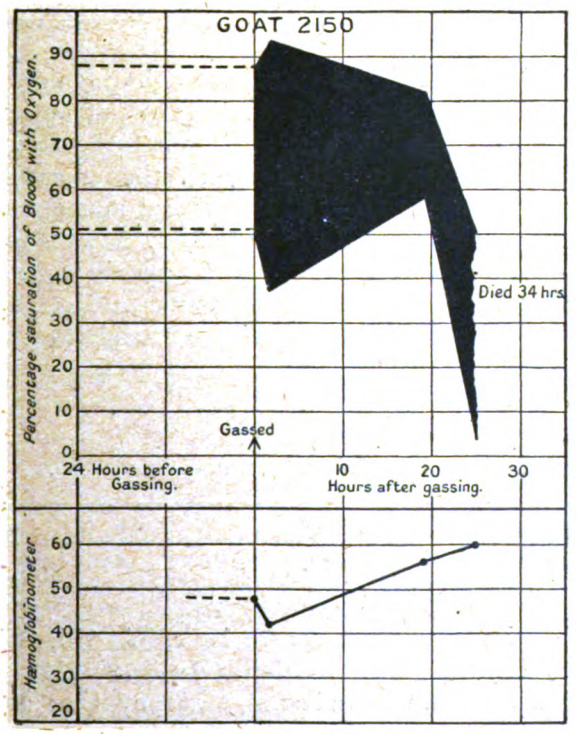

FIG. 8.

(*a*) The respiratory system relapsed not quite to its normal ventilation.

(*b*) The circulatory system failed, so that the venous blood, instead of being more red than normally, became more black, and the minute volume sank to 2¼ litres.

Why did not the animal sink, too? Probably because the position as regards anoxic anoxæmia had become consolidated by this time.

---

[1] The oxygen which leaves the blood is expressed by the depth of the black area, normal 96 — 41 = 55; at nineteen hours, 93 — 65 = 28.

(*c*) I say "consolidated" advisedly, because the fresh unit to come into action was the shutting off of the more damaged parts of the lung. The alveoli most affected became consolidated, and the blood practically ceased to flow through them. The alveoli least affected cleared up. The goat may be regarded simply as having had a small lung; but the animal had made good as regards the aeration of the blood which traversed it.

The conditions of anoxæmia, therefore, at the twenty-fourth hour are :—

ANOXÆMIA TWENTY-FOURTH HOUR.

Type 1	Type 2	Type 3
Anoxic.	Anæmic.	Stagnant.
Nil.	Nil.	Profound.

A little more thought may be spent upon the inquiry, "What would have happened if this goat had not been able to put up a successful fight against the anoxic condition?" The answer is to be found in goat 2150 (fig. 8). During the first nineteen hours, the anoxic condition was gradually making headway, so that at the critical moment when the circulation gave out the arterial blood was but eighty-two per cent oxygenated. And then a vicious circle was set up. To the anoxic anoxæmia was added the stagnant anoxæmia, which in turn reacted upon the respiratory centre. The centre became more and more feeble, the respiratory rhythm weaker with a corresponding deficiency in the power of the lung to aerate the blood, and so by the end of twenty-five hours the conditions were :—

Goat 2150.

CONDITIONS OF ANOXÆMIA TWENTY-FIFTH HOUR.

Type 1	Type 2	Type 3
Anoxic.	Anæmic.	Stagnant.
Profound.	Nil.	Profound.
	(Hyperæmia of.)	

The animal died at the thirty-fourth hour. At this point let me say something about oxygen administration. In goat 2150 oxygen would probably have been used with advantage at any time after the eighth or tenth hour, but the reasons for giving the oxygen would have been different at different times. Up to the nineteenth hour the reasons for giving oxygen would have been largely preventive. The oxygen would have warded off the anoxic condition and therefore

(*a*) postponed the collapse of the circulatory and respiratory systems.

(*b*) prevented the formation of the vicious circle by reason of which the stagnant and anoxic types of anoxæmia combine to reduce and finally extinguish the respiratory centre.

After the nineteenth hour the administration of oxygen is not to obviate the formation of the vicious circle but to break it, the oxygen is to cure not to prevent—to light up the respiratory centre once more. Indeed, not only is the condition of the respiratory centre improved, but that of the

whole brain, so that the patient who has been semi-moribund and therefore quiet at first becomes restless, and so may give the impression of becoming worse when he is actually much improved.

It may seem that a good deal of what I have been saying is rather unpractical. You may ask: "What are the indications of the various types of anoxæmia which you have been describing?" How, for instance, am I to discriminate as between the conditions corresponding to those of goat 2150, at the nineteenth and twenty-fifth hours respectively? One very important indication is to be found in the nature of the cyanosis. So long as the circulation is making a fight the cyanosis will be of the plum coloured type. Twice the normal amount of blood is traversing the body, the vessels are dilated as in exercise, but the blood in them is not the ordinary red colour of the blood which traverses the skin areas of an active person. It is more purple. The heart is probably somewhat dilated. This is the condition of "plum coloured" cyanosis. It is in this condition that oxygen is given as a preventive.

The condition of livid or grey cyanosis is the much worse one in which the circulation has failed, and in which the respiratory centre is fast failing, the respirations being shallow and feeble, the heart rapid and thready. The patient, unless the course of events can be altered, will go out.

Let me now put before you the evidence that oxygen really does good. I append two quotations from the actual experience of officers who have administered it in the field.

The first is one in which it was given at a late or collapsed stage:—

EXTRACT FROM CHEMICAL WARFARE, MEDICAL COMMITTEE REPORT No. 10.
Page 12. *Case* 2 (*reported by Lieutenant-Colonel Douglas*).

Day 1.—Gassed 6 a.m. by gas shell (? tri-chloro-methyl-chloroformate). Reached casualty clearing station at 10 a.m. Treated with intermittent administration of pure oxygen. 9.50 p.m.: Pulse hardly palpable, impossible to count rate. Livid cyanosis. Patient in a very grave condition and appears moribund. Five litres oxygen per minute by Haldane apparatus causes considerable improvement in colour, but even with ten litres per minute the colour does not become quite normal. Continuous administration of six litres of oxygen per minute started, the mask not being removed for more than a minute or two every half-hour. Pulse becomes palpable after a few minutes, but its quality fluctuates, rate 120. Half an hour after starting oxygen, respirations 52, not deep.

Day 2.—1.30 a.m.: Pulse 112, still very weak, but regular. Respirations 58. Patient objects to having the mask removed. 3.30 a.m: Pulse 108 and slightly stronger, respirations 58. Patient tries to prevent mask being taken off, as he can sleep so long as he is having oxygen. 5.30 a.m.: Pulse 108, respirations 56; colour of face while oxygen adminis-

tered is definitely better than it was before. 8 a.m.: Pulse 100, respirations 54. Five litres of oxygen per minute cause a marked improvement in colour, but with three litres per minute there is not nearly so much relief of the cyanosis. Oxygen administration continued at five litres per minute. 9.30 a.m.: Pulse is still weak, though definitely stronger than at the start: rate 102, respirations 48. Patient more conscious and does not look so moribund while oxygen is being given, but when the oxygen is stopped his condition deteriorates rapidly, with return of marked cyanosis. The oxygen treatment was continued subsequently. This patient eventually made a good recovery. It was possible to transfer him to England on the tenth day, and he re-joined his regiment in France within a year.

In the second the oxygen was given in the early or plum-coloured stage of cyanosis :—

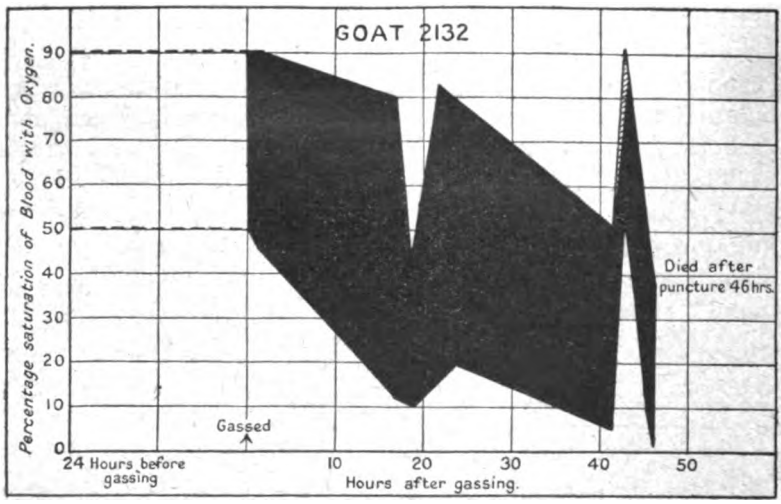

FIG. 9.

Page 13. *Case* 4 (*reported by Captain Peters and Captain Bevan*).

Day 1.—Gassed with chlorine at 2.13 a.m. Treated with inhalations of ammonia and steam at once. 4 a.m.: Slight cyanosis; respirations 26, pulse 88. Treated with intermittent oxygen till 5.45 a.m. 5.50 a.m.: Arrived at field ambulance. Respirations 40, pulse 76. Cyanosed. Two litres of oxygen given by Haldane apparatus for ten minutes every half hour till case reached casualty clearing station. 7.30 to 11 a.m.: Cyanosis relieved by two litres of oxygen per minute by Haldane apparatus. Rhonchi and fine râles audible in chest; slight dilatation of right side of heart; respirations 24, pulse 80. Two litres of oxygen per minute given for twenty-five minutes every half hour. 11 a.m. to 1 p.m.: oxygen given for twenty minutes per half hour. 1 to 6 p.m.: Periods of oxygen administration gradually shortened.

Day 2.—Oxygen administration stopped. Area of cardiac dullness now normal. Patient made a rapid recovery. These reports fully justify the prolonged and continuous use of oxygen by a proper method, and the pushing of its administration in a great enough concentration until cyanosis is relieved. It appears to be of value in both the "grey" and "plum-coloured" types of cyanosis.

The question may quite reasonably be asked, "Has oxygen really access to the blood in the later stages of gas poisoning?" In answer to this question let me show you two figures; the first is that of a goat which was practically moribund forty-one hours after being gassed (goat 2132, fig. 9). The oxygen in its arterial blood had fallen to forty-five per cent, and in the venous blood to five per cent of the total possible

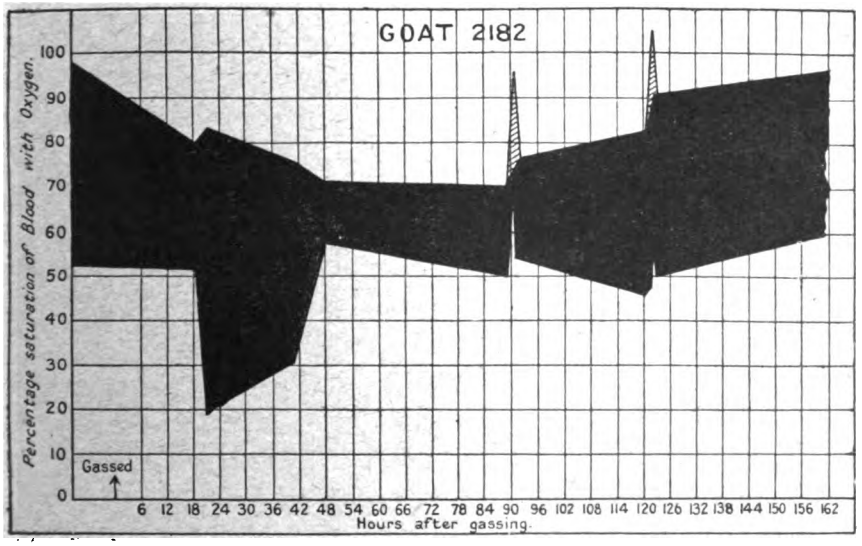

FIG. 10.

content. He was given oxygen to breathe for thirty minutes. Whilst breathing the gas the oxygen in the arterial blood rose to ninety-two per cent and the venous to fifty per cent, almost exactly the normal percentages. Clearly, then, the oxygen "got there," and it is important to note that even after the administration of oxygen ceased the respiration was improved to such an extent that the oxygen in the arterial blood was eighty-four per cent. But, as Haldane says, anoxæmia "not only stops the machine but wrecks the machinery." The goat was too far gone to be saved by half an hour's respiration of oxygen, and it presently sank to its former condition.

A more encouraging and no less instructive case is goat 2182 (fig. 10), which at the end of ninety hours from being gassed was in a very anoxic condition, the oxygen in its arterial blood being seventy per cent. After

administration of oxygen for an hour the quantity of that gas in his arterial blood was ninety-six per cent while the gas was being breathed, and that in the venous blood rose to sixty-eight per cent. Moreover, the arterial blood never again fell below seventy-seven per cent, so far as we know, and from that point the animal improved. Another spell of oxygen breathing took place one hundred and twenty hours after gassing. This spell of oxygen respiration lifted the animal a step higher, after it the oxygen in the arterial blood was ninety-two per cent. At the end of one hundred and sixty-two hours the oxygen in both the arterial and

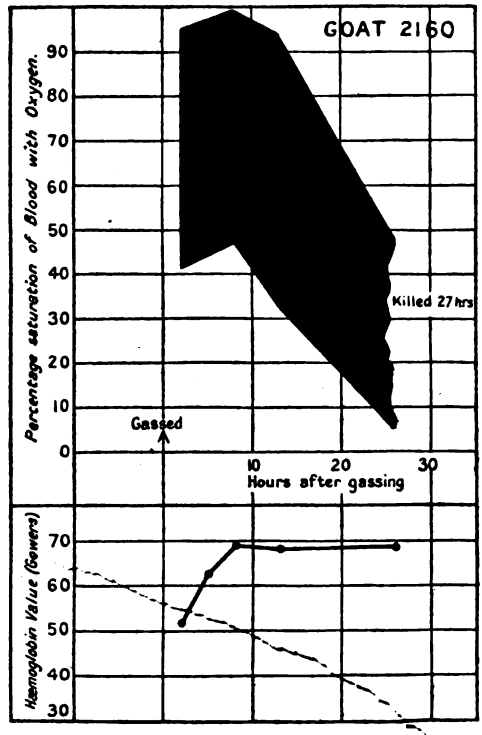

FIG. 11.

venous blood, was normal. The animal appeared also to be well and not in any way fighting for its life.

In my discussion of goat 2150 there was one point over which I passed rather lightly; the anoxæmia position, you will remember, was as follows:—

ANOXÆMIA.

Type 1 Profound.	Type 2 HYPEROXÆMIA.	Type 3 Profound.

The word hyperoxæmia in column 2 signifies that there was a notable increase in the number of red blood corpuscles in each cubic millimetre of

blood, and consequently a corresponding increase in the quantity of hæmoglobin present and of oxygen carried by it.

Another case in point is goat 2160 (fig. 11). At the bottom of this figure the hæmoglobin value of the blood is plotted. When gassed this was fifty-eight by the Gowers scale—quite normal for a goat. As this case ran its course, the hæmoglobin rose to 70; in other words, the blood became concentrated in the ratio of 70/52, or roughly 7/5 or 140/100. Each cubic centimetre of blood contained forty per cent more corpuscles than it would otherwise have done. From the point of view of anoxæmia then a very interesting situation arose about the twentieth hour. On the anoxic count the blood contained about forty per cent less oxygen than normal because it was unsaturated to that extent; on the anæmic count the blood contained forty per cent more oxygen than normal because there were forty per cent more corpuscles. Taking the two together the actual amount of oxygen in the blood was that of the normal goat. Therefore you are faced with the question: Was there really any anoxæmia at all? Does the hyperoxæmia due to concentration compensate for the anoxæmia due to want of oxygen pressure in blood? The point may seem to you rather subtle, but in reality it is not so; moreover, the correct understanding of it is most fruitful from the point of view of treatment.

It cannot be too clearly stated that the hyperoxæmia contingent on concentration does not compensate for the anoxæmia resulting from the anoxic or unsaturated condition of the blood. Calculations recently made for me by my colleague Mr. F. J. Roughton, of Trinity College, Cambridge, indicate, indeed, that concentration compensates so little for unsaturation, that if there is anything to be gained on counts by getting rid of the concentration, the way is perfectly open to do so.

The concentration of the blood is of course caused by the abstraction of water from it. The fluid goes in part to form the œdematous exudate in the lung, and possibly, but not certainly, in part into the tissues. The destination of the fluid is, however, in the present discussion immaterial, the point is that the volume of the blood is reduced beyond the danger point. If, for instance, goat 2160 normally had a blood volume of two litres, at the moment of death it would have a blood volume of but 1·5 litres. The dangers of this condition were discussed in a lecture given in the Royal Army Medical College by Professor Bayliss last year. The immediate treatment demanded to compensate for it is the intravenous injection of saline in such quantity as will restore the blood volume. The treatment of gas poisoning by venesection and subsequent intravenous injection of saline solution was worked out with great care in America by Professor Underhill, and to some extent at Porton by two American officers, Lieutenants Goldschmidt and Wilson, sent over to Europe as part of the United States organization. In parenthesis I should like to say that their presence on my staff is to me a very happy recollection. The American treatment, in so far as it was directed against anoxæmia at all, was directed

solely against the stagnant type. The early bleeding to counteract the possible occurrence of high blood-pressure on the right side of the heart, with the consequent slowing of the circulation owing to increased back pressure, or *vis a fronte*, the subsequent injection of saline to increase the blood volume at the moment when its loss means a lack of arterial pressure or *vis a tergo*.

The success of the treatment so far as can be gleaned from experiments on animals is shown by the following table :—

	Deaths in first three days per cent	Delayed deaths per cent	Survivals per cent	Number of animals used
Untreated	57	17	26	23
Treated by bleeding and infusion of saline at time of marked hæmoglobin concentration	22	5	73	23

Let me, in the minutes which remain, recapitulate shortly what I have said about treatment.

Three different types of treatment have been cited :—

(1) Bleeding and infusion of saline.

(2) Oxygen treatment.

(3) Rest (which includes warmth).

The *raison d'être* of each hinges on anoxæmia in part at all events.

Infusion seeks to combat the stagnant type of anoxæmia by restoring the volume of the blood and re-establishing the blood-pressure; it aims at securing the circulation of an adequate supply of hæmoglobin throughout the tissues.

Oxygen treatment combats the anoxic type of anoxæmia directly, and therefore if given early wards off (*a*) The loss of power of the respiratory centre, which would lead to an even more profound anoxic condition; (*b*) the onset of the stagnant type caused by heart failure.

Rest, which reduces the oxygen requirements of the body to a minimum and thus reducing also the anoxicity, avoids sudden vagus stimulation of the heart or the necessity for rapid vasomotor accommodation.

These three lines of treatment, touching as they do different phases of anoxæmia are not interchangeable. Ideally they should all be prescribed; in practice the ideal must be aimed at, and in so far as circumstances permit, attained.

FRAGMENTS.

By Colonel Sir ROBERT FIRTH, K.B.E., C.B.

X.

Probably few will be prepared to deny that a prevailing feature of our present-day social and sartorial customs is pretentiousness, or an attempt to pass off the artificial as the real. The truth of this generalization was pressed forcibly upon my notice to-day, when travelling in a Tube railway carriage. Seated in a row before me were seven females of various ages and degree. Each one of those females wore some kind of fur garment, and I think I am correct when I say that only one of those females wore a fur made actually from the skins of the real animal from which the fur was professed to have been made. All the other furs were imitations. What sacrifice of life that pelt-clad row of females represented I was reluctant to think, though convinced that no one of that row had ever given such sacrifice a moment's thought. My interest focused mainly upon the solitary genuine fur before me, as it was uncommon and a species very difficult to imitate. As a matter of fact, the article was an ermine stole, and, from the general appearance of the wearer, probably a well-guarded relic of more affluent times. That stole fascinated me, and as I sat there looking at it, I tried to calculate how many skins of the *Mustela erminea erminea* from Scandinavia or Russia had gone to make up that British female's wrap. My estimation made the number to have been between seventy and eighty.

From this prosaic fact my thoughts wandered not inconsequently back to my boyhood days when I was familiar with similar little beasts, and once outraged the gentility of some of my relations by bringing home a member of the ermine family as an intended pet, only to find myself forbidden to approach near the family circle until my garments had been deodorized. I fancy neither the female who sat before me nor few of those who wear expensive ermine realize that they are adorning themselves with the skins of animals that are for practical purposes identical with the common stoat of our country side or *Mustela erminea stabilis*. The essential difference is that the ermine of Scandinavia and Russia, and also the *Mustela erminea cestiva* of other cold regions, turn white in winter, save the tip of the tail which remains black or very dark brown. The British stoat rarely changes colour in the winter, because a white dress would possibly make him much too conspicuous in these islands. An exception may be made of stoats in the north of Scotland, where, owing to the winter being colder, the change in colour certainly takes place. I have seen a perfect "ermine" in Hertfordshire once, and often other stoats showing more or less of white during winter in the same county when I was a boy,

but they were rare. On the other hand, stoats killed in mid-winter often show an increased amount of white round the muzzle, which is where the transformation begins and gradually extends to the rest of the body, if the change do occur. The one white stoat which I have seen was certainly a fine fellow, and his beautiful ermine coat was conspicuous against a background of brown bracken and grass. I remember well the excitement which his presence in a certain coppice aroused among my intimates and the futile efforts some of us made to secure so rare a specimen. Doubtless he has been dead quite forty-five or more years, but now, as I think of him, I hope he ended his days as a good stoat should and was not caught in some snare or trap. It is a common belief that this mimicry or assumption of a white pelt in northern regions to match the snow-covered environment is but a device to render the animal less visible to its prey and to its enemies. It has its analogy in many other forms of life, especially among the Lepidoptera, and more particularly among the so-called "stick" caterpillars of Ceylon which are so like twigs that many persons pass them over as nothing but inanimate pieces of wood. But the retention of the conspicuous black tip to the tail of ermine suggests a doubt whether mimicry is the real cause or reason in their case, and this doubt is emphasized when we remember that the majority of northern mammals, be they formidable and strong like the polar bear or weak and defenceless like the northern hare or the Arctic fox, adopt the same white coat. May it not be that there is some correlation between white coloration and the ability to withstand great cold? Whatever the reason may be, it is evident that the ability to turn white in winter and to resist cold has been more or less lost by the English, Irish and southern continental stoat.

Certainly, the stoat is a mighty hunter, but I have often wondered why he is singled out as the foremost among creatures which the gamekeeper ranks as vermin. When the stoat hunts, he hunts only for food; he never kills wantonly, neither does he kill more than he wants. Can the same be said of man who kills scores of rabbits and birds for mere amusement? Essentially, the stoat is no worse and certainly he is better than his human persecutor in respect of the quantitative butchery which he commits. If the stoat be really a criminal and an outlaw, then the crime of which he is guilty is not that of being a cruel murderer but simply that he competes with us for what we want ourselves. It is a lamentable conclusion to reach, and yet indisputable. Like all creatures that live by their wits, by hunting others, the stoat is a spritely little fellow. Every man's hand is against him, yet he seems not to care, but skips between the grass tufts or slips into the bushes and vanishes like a fairy. Often have I watched his gambols and noted how full of curiosity he is, for, if not too seriously frightened, the stoat will always come back to have a look at whatever it was which disturbed him. Too often this inquisitiveness is his undoing, because it is a favourite dodge with keepers, when a stoat has escaped them, to stand and wait and promptly shoot when the little

animal comes back to have a second look. Stoats vary much in size, but the males are generally 11 inches in head and body length, with 4 to 5 inches for the tail. The females are smaller, averaging from 9 to 10 inches long, with a tail of 4 inches. They are frequently confused with weasels, but the stoat can be known always by the conspicuous black tip to its tail which the weasel never possesses. The long lithe body and short legs of the stoat enable it to move by a series of bounds; it moves like a flash, with sinuous grace, and its black tipped tail flirting behind it as an impudent challenge suggesting "catch who catch can." He is a plucky little fellow, especially in defence of his young, has sharp teeth and also the ability of emitting, when in difficulties or danger, an odoriferous fluid from the anal glands. This smell is unpleasant to a degree, and constitutes a very real form of defence, especially against dogs, on whom it has a definitely intimidating effect.

The chief victims of stoats are mice, rats, young birds and rabbits. They have been known to take eggs. Stoats are not particular as to where they live; as a rule, a hollow tree, a crevice in a wall, a rat's hole, or any snug dry retreat suffices them either as a sleeping place or as a nursery. The breeding season is usually in April or May, and the young are extremely difficult to find, as the parents will dare anything in their defence, and, if suspicious of danger, do not hesitate to carry the young ones off to a fresh nursery. As the number in a litter is six or seven, the family when on the move or out on an educative foray, make quite a large party, and to watch their lithe quick movements is delightful. In attacking rabbits and other animals, the stoat invariably kills by biting at the neck. It is astonishing what a terrifying influence a stoat has over a hunted rabbit or other creature. I have often seen such a rabbit quarry both hunted and killed. The extraordinary thing about it all, especially in the case of rabbits, is the crass stupidity of the rabbit. When a stoat enters a burrow, the inhabitants give an alarm signal by striking the earth with their heels and then bolting in all directions to gain the surface and open country. If they only ran right away they all would escape, but, instead of doing that, they stop after going a short distance, sit up and listen or look back. This is fatal, as the stoat quickly picks up and follows the trail; he singles out one trail or scent and sticks to it. The wretched rabbit, on whose track he is, suddenly alive to danger, makes another short run and then crouches down with ears back hoping to be invisible. The scent is strong and up comes the stoat, away goes the victim once more, but, by now, he is paralysed with terror, seems unable to run, rolls over with a cry and, although unhurt, lies helpless awaiting the *coup de grâce* from the flashing mass of brown fur which hurls itself upon it and promptly snaps the spinal cord by a vicious bite over the back of the neck. Occasionally, even the final bite is not needed as rabbits have been known to die of fright when hunted by stoat or weasel. The only time a rabbit will show fight is when a doe has young near by. Under such circum-

stances even a rabbit will face a stoat, and what is more, very often beat the hunter off. It is always a doe who shows fight, and she jumps over the stoat or weasel, dealing sharp blows with her heels. She will stick to the hunter, hitting him again and again until he is only too thankful to rush off and escape the buffeting. I have never seen these frays myself, but often have heard first-hand descriptions of them from those who have seen for themselves. From all accounts, the stoat seems to come off second-best usually. If he does, I fear he takes ample revenge when the breeding-time is over and mother love less able to assert its power.

Some points of interest are associated with the geographical distribution of the ermine family. The common stoat of Great Britain, *M. e. stabilis*, does not seem to be identical with the Irish stoat, *M. e. hibernica*. This latter is said to be smaller and without the white edging of the ear and upper lip which is so characteristic of the British stoat; also the brown of the sides of its body extends over or reduces the white or cream coloured patch which ordinarily covers the throat and belly of the British type. The same features mark the stoat of the Isle of Man, and it has been suggested that the Irish and Manx stoat is a distinct species. If this be so, then why should the Isle of Man and Ireland have a stoat peculiar to themselves? The only explanation is that when, at the close of the last glacial period, the snow and ice retreated before a milder climate, these islands were a part of the European mainland and the animals followed up the retreating ice. While this was going on, subsidences occurred giving rise to the Irish Channel, with the result that the Isle of Man and Ireland were separated from Britain, and such mammals and other creatures as had moved forward to reach the two first named islands became isolated. Amongst them must have been the ancestral stock of Irish and Manx stoats. We know that the fauna of Ireland is much more limited than that of Britain, and that many creatures like moles and snakes never got so far as where Ireland is now and that, though Britain has them, Ireland is without them. When the separation took place, Britain was still attached to the mainland, and for that reason she has continental species that never reached what is now Ireland. That this is the real explanation is confirmed by the fact that, not only among the stoats, many British species are more closely allied to those of the mainland than to Irish ones.

Thus, the lady with the ermine stole has led me to think and write of stoats. Not a very popular creature in life to most people, but still, to those familiar with the life of hedges and ditches, a very interesting, beautiful and graceful animal, a mighty hunter, a foe of the game-preserver, but for all that a real friend to the farmer. I leave it to the reader to judge the little creature on his merits, with the parting plea that it be not forgotten that the stoat holds a place in our fauna from which we can ill afford to drive him, and that to him and his kind we owe that balance of Nature which saves us from being overrun with rabbits, voles, rats and mice. His memory is better kept by a woman's tippet than by a keeper's gibbet.

XI.

The unexpected but welcome find of some Treasury notes in an overlooked pocket, coupled with a severe attack of boredom, induced me lately to indulge in a round of visits to theatres. It is a form of amusement which has never appealed strongly to me, and my recent experiences have not tended to make me change my ideas. Be that as it may be, certain reflections have asserted themselves. In the first place, the drama and the stage are not synonymous terms, neither are the drama and the theatre. The art of the theatre is a composite art with endless ramifications, and probably the audience is not the least important element, but the quality of the audience is not a thing which is controlled by any side of the theatrical profession. The audience is an unknown quantity and will remain so until play-writers and play-actors have achieved a surer measure of the psychology of the public than they possess at present. The cause of that failure is probably due to a forgetting that the drama is an art with powerful educational and social reactions. The social aspect of the drama is as old as the drama itself, and anyone who knows anything of the early history of the art realizes that its connection with social life was recognized by the political and religious leaders of those days. Those familiar with Greek drama know that dramatic performances were organized annually by the State as part of the official ritual of celebrations of tribal worship and, coming down to more modern times, drama was ever the handmaid of religion throughout the mediæval period, while, in Elizabethan days, drama was held in such educational esteem that it was accorded a place in the regular courses of school and university study.

We, in this day, seem to have lost sight of the educational value of the drama, more especially of the dramatic method as an item in general or non-vocational education. Much might be done by the organization of opportunities for children to see good plays acted and by encouraging children themselves to act plays as a means of acquiring means of self-expression and training in the art of speech. How great is the need of this latter is only too apparent by the distortions of our mother tongue forced upon our ears in any public vehicle. Apart from its elocutionary value, play acting is an incentive to spiritual understanding, for to act a part with sincerity is to throw oneself into the point of view of another person; play acting also helps to overcome for a while the limitations of the individual self and to gain a glimpse of the broader view which comes to those who have learnt to use the gift of imagination. It is questionable whether our ordinary methods of education do anything to encourage or instil this attitude among the younger generation, and it is an attitude of mind of which our present world is sorely in need.

There are not wanting signs of an appreciation of this urgency among those anxious to construct a new educational policy in this country, but their efforts will be useless and unavailing without a

parallel movement, which shall ensure at our theatres the performance of good plays for the adult as well as for the child. My recent experiences suggest that there are no present-day signs of such a parallel movement; on the contrary, to go to most of our theatres means too often the paying of a high price for the privilege of getting a seat from which one is forced to listen to vapid banalities. It cannot be repeated too often that drama is an art and, if it is to maintain itself as such, its true nature must be kept steadily in view, and that nature is inseparable from a complete integrity both of aim and impulse. It would be uncharitable, perhaps, to say what appears to be the aim and impulse of many dramas and pieces now staged. For thus hinting at what are my own impressions, I disclaim any spirit of censoriousness or hyper-criticism wishful to suppress what may seem undesirable at the expense of the legitimate demands of popular entertainment, but I advance a plea for a really constructive sense of the value of the theatre and to utilize its power to unite and inspire human minds through the shared experience of noble ideas. To amuse himself sensibly is one of the distinguishing marks of civilized man, and in this refining of the recreative sense the theatre should play a large part. Even from the artist's point of view the education of the audience is the prime necessity of the modern theatre, but we cannot expect any considerable advance in the standard of the popular play till the public, as a whole, has learnt to regard the best as a normal, and not as an abnormal, production. How many of those who may read these fragments can say they go to a Shakespeare play really because they appreciate its worth, and not influenced by the prestige which still makes the bard of Stratford fashionable? I am inclined to think that but few could answer truthfully that they go from the higher motive. Why? Is it because they are less educated than were the Elizabethan public? Certainly not, but merely less cultivated in their sense of drama and less able to assume the right attitude to drama as an art. It comes, therefore, to this, that the education of a modern audience can only be effected by familiarizing it persistently with the best, and this is just what my recent round of theatre going compels me to think the present day theatre fails to do.

It would be untrue to say that there have been no thought-stimulating or good plays produced in recent years; there have been several, but they have been as oases in a desert, few and far between. It would be equally unjust to blame the directors of theatres for this; theatres are not charitable institutions, but undertakings run for profit, and the management supplies naturally only that which it thinks will attract profitable audiences. The public is catered for in terms of its supposed or declared taste. It is here that we find the root cause of an apparently decadent drama. The patrons of the theatre exist in their hundreds of thousands, but it would appear that they are highly indifferent to any aspect of stage art save that of its quality of sheer amusement. Outside small cliques here and there it would be hard to find a seriously interested public for

theatre performances in the same sense as there is a serious public both for music and painting. By way of contrast there are the vast hordes who fill the cinema halls. These are they who will tell you that they have contracted the cinema habit and flatter themselves that they have acquired a faculty of literary and dramatic criticism, whereas, by the constant feasting upon crude facts and reality, they are steadily withering their faculty of imagination and putting their minds to sleep. No lover of the dramatic art will submit to the view that the film can ever take the place of the actual play. There is no art in this business of cameras and claptrap. It is made by artifice and run by skilled mechanics. Its so-called acting is but a mixture of inane tricks, portentous grimacing and heavy-footed movements. All this is far removed from the living flesh and blood which provides that medium for spiritual expression which is the unique privilege and glory of the art of the actor. All that is a thing for which the realism of the film can be no adequate substitute, and the contraction of the cinema habit differs as much in nature and value from the cultivation of the sense of drama as the intellectual value and education gained by translating a piece of Latin or Greek by means of a crib differs from that derived by construing the same with the aid of a dictionary.

When I recall some of the fine plays which I have seen, where every gesture says something in conjunction with the spoken words, and wherein is built up an atmosphere suggesting intellectual thought and the calling into play imagination, the crudities of the cinema performances are magnified twenty-fold. Or, take the simple case where an author, in the course of his story, throws in a suggestion that a wife or child is ill-treated by the man: an atmosphere is created, and, if the author and the actors have suitably conveyed that atmosphere, the reader's or onlooker's imagination is clothed with it, and he is filled with pity at the half-known thing. But when cinema pictures show a brutal man striking wife or child with a dog-whip, art is left out and the audience suffers nothing of that pity, only nausea remains. If the audience be a child audience, the damage done by these cinema pictures, even if of the wholesome type, is enormous, because they rob the child of to-day of the exercise of that precious faculty—imagination. In the cinema, children are shown every detail of a given situation; there is no opportunity for wonder and no suggestion round which their minds can play. Not for a moment are they allowed to think, for every small idea is explained and illustrated until the mind slumbers. The screen shows everything in crude unsatisfying reality, the audience is given the bare substance and robbed of the delicious enduring shadow. The cinema habit is like the short story habit, an outward and visible sign of a public too indolent to think.

The question arises on what lines or by what methods can the dramatic sense be cultivated among the public? The answer depends much upon whether the people, in their collective capacity, will ever be likely to regard the drama as of sufficient importance, whether as an art or as an element

in social culture, to be worth the public recognition which is not grudged to literature by way of free libraries, to art by way of national and municipal picture galleries, and to music by way of bands and band-stands. Given sufficient time to think about it, I believe they would, though doubtless some opposition would arise on the plea that a national or a municipal theatre is an expensive luxury. The reply is, surely, that the expenditure would be trifling compared with the vast sums now spent on cinema halls and the contemplation of pictures dealing with the underworld and the side issues of our marriage and divorce laws; whereas, the sphere of influence represented by a theatre presenting only the masterpieces of British and foreign drama, ancient and modern, would be infinitely wider than that of a free library and of far more varied cultural value than that of an art-gallery or a municipal band-stand. While painting and music are mainly æsthetic in their appeal, drama is bound up with the whole moral and spiritual fabric of human life. Not merely for the sake of the nation and the intellectural culture of the people, but for the sake of the art of the theatre we need a national temple of drama. All may not agree with me, but I conceive worse forms for a national war memorial than a national theatre. Whatever its merits, or demerits, it would certainly fulfil the fundamental conditions of being permanent, useful and democratic and, if dedicated in the name of Shakespeare, would be a fitting memorial of Britons' noblest effort to transmit unimpaired to posterity his spirit and theirs.

XII.

"Pray, doctor, let me know whether writing letters be talking to ourself or talking to other people?" Anthony Hurley asked this question of Jonathan Swift two hundred years ago, and the question still remains unanswered. I have put this same question recently to my friends, and the general answer is, "Of course, we are talking to other people," the reason offered being, because we write differently to each of our friends. I am doubtful whether it is altogether a correct or satisfying answer and would suggest to the reader the fascinating speculation of trying to trace how much of the charm of a letter is due to the writer and how much to the reader at the other end of the post. Possibly, little of a letter's charm is due to either but rather to the actual subject matter and the manner in which it is conveyed or expressed. In fact, the truth is probably hinted at by Cardinal Newman, who wrote, "Biographers vanish, they assign motives, they interpret Lord Burleigh's words, but contemporary letters are facts." And this brings me to my theme, which is not to write about other people's letters but about biographies, especially autobiographies, two of which I have been reading recently, namely Rousseau's "Confessions" and Barbellion's "Journal of a Disappointed Man." The two books, like the two men, differ widely in nature and style but afford much material for quiet thought. The latter is an astonishing book, the picture of a man who might have

become one of the greatest of English biologists, a picture superbly drawn by himself.

Why, we may ask, are autobiographies written? The trait common to all who have written the story of their lives is the expression of self-preserving instinct or the effort to persist in one's own being. Some may write, as Rousseau did, from the sheer impulse of self-confession; or like Barbellion, as one who feels that in the self he has something of unique value to give; or, like Newman, as one prompted to self-defence; or, like the memoirists, they thrill to their impressions of the features of the great road along which they have travelled, but each and all stand committed to affirm themselves and to save their own souls and lives out of the wreck of changes. And we, who read these records, get a picture of the real nature and spirit of the man which in the real life was constantly missing, because in life we are too distracted by the cross currents to recognize them. In autobiographies, we see the man and his nature as a whole; these complete pictures of men and women we do not get from biographies because the biographer, with the best intentions and the subtlest insight, can only give a second-hand portrait. We all know how the individual seems missing among many whom we know and meet, we also know that our own individuality is not always realized even by ourselves. The great charm of a good autobiography is that it reveals this possession, since the desire to survive is a desire to survive as oneself and not as another. Those who write autobiographies attest their own existence as individuals, and those who read them appreciate their value, because they find in them a common humanity minutely pictured. We do not respond equally in all cases, being moved sometimes by the sense for truth, sometimes by circumstances or temperament, and sometimes because the historical sense gets in our way. For all that, we recognize a good autobiography to be life at first hand and often as the explosive assertion of a personality.

The "Confessions" of Rousseau are a remarkable example of the kind. In that book we come face to face with a man who awakes the sense of universal truth and yet is at the same time defiant. He goes out of his way to show that he is doing something which has no precedent, but is obviously trying by his self-assumption for uncompromising truth. There is an element of vanity in him, but he shows himself to be the first of the insulted and injured, for proud of his consciousness of his genius, strung by real and imaginary misfortunes, thirsting for an unattainable tranquillity, he makes a glory of his shame. There is no concealment or glossing over of moral abasements and secret physical infirmities but, wholly unabashed and confident of his essential goodness, Rousseau has the temerity to invite us to follow his example and then say, if we can, that we are better than he. The purely morbid attraction of this book is great and there are many who regard it as the work of a madman. Certainly, Rousseau was a neurasthenic, but the great claim for his "Confessions" rests on his sincerity and that he devoted his genius to making a self-portrait in all the nakedness of

truth with the demand that this truth and nothing short of it was the duty of a writer. A claim of this kind gives us a shock and challenges the moral judgment; but are we in a position to give moral judgment? The true autobiographer puts all his cards on the table and shows all; we show nothing and attack him for what he shows. If we sit in judgment we must also in the same measure judge ourselves. By this, I do not mean that we should all be autobiographers, but that in reading the autobiographies of others we should submit ourselves to the same exposure as they have submitted themselves. Having done that, it is questionable whether we shall feel inclined to pick up such scraps of morality as remain, but rather be prepared to admit that we have not all the qualifications for filling the judgment seat. This seems to be the essential lesson to be drawn from Rousseau's "Confessions," which are the complete emergence of a person and which, under a mask of egoism, conceal the soundest rule of guidance in these matters.

The same note of defiance is sounded in a passage in the "Journal of a Disappointed Man" by Barbellion, wherein he bids us come out of the defences where we skulk. It is a very different kind of book to the "Confessions" of Rousseau and written by a very different type of man, but the book is a "self-portrait in the nude." He says, "I am apparently a triple personality: (1) The respectable youth; (2) the foul-mouthed commentator and critic; (3) the real but unknown I. Curious that these three should live together amiably in the same tenement"; and the last words in his journal are, "Friends and relatives say that I have not drawn my true self. But that is because I have taken my clothes off and they cannot recognize me stark! The book is a self-portrait in the nude." In actual fact, Barbellion was a man who, from boyhood, had been weakened by continual ill-health; his journal is full of medical notes and forebodings, but few realized how constantly the fear of sickness and death attended him. He never mentioned his health save in a tone of cheerful cynicism, he never pampered or spared himself, but worked unceasingly keeping his balance and his courage under staggering blows of ill-fortune. Never was there so impossible an ambition as that of this sickly youth in Plymouth, already chained to the dreary work of a reporter to a provincial paper, who desired, without help or any decent opportunities for self-instruction, to obtain a scientific appointment. Yet he overcame these obstacles and fulfilled his ambition by first obtaining a post in the Plymouth Marine Laboratory and then winning in open competition an appointment in the Natural History Museum which justified the abandonment of journalism. Ill-health dogged his steps, and when nothing was left but a few months of painful life and his journal, he continued the self-portrait which had become his last ambition as long as he could hold a pen.

Reading that journal, it is not difficult to understand the complaint of his friends and relatives that he had drawn a misleading portrait of himself, any more than it is difficult to understand his own protest that he had

drawn himself with the clothes off. Both points of view are natural and we need not involve ourselves deeply in the theories of psycho-analysis to emphasize the opinion that a man who keeps a journal will use it largely to put down what he cannot say anywhere else, and to express that aspect of himself which cannot be expressed in the ordinary world. No man who is a hero to himself stands much chance of seeming a hero to other people, but the following passage makes Barbellion's journal an extraordinary document: "I can never marvel enough at the ineradicable turpitude of my existence, at my double facedness, and the remarkable contrast between the face I turn to the outside world and the face my friends know. It is like leading a double existence. If only I had the moral courage to play my part in life, to take the stage and be myself, to enjoy the delightful sensation of making my presence felt, instead of this vapourish mumming, then this Journal would be quite unnecessary." This passage refers to his admission of a want of personal courage and his inability to express and display his contempt of stupid and overbearing persons before whom he quails and presents only a timid exterior. He is aware of the contrast between what he allowed the world to see and the rest of his nature, but this contrast remained mysterious to himself, leaving something over of which he was ignorant. And yet throughout this interesting Journal there bubbles up the man's evident effort to persist in his own being, which self-preserving instinct is the primal motive of all autobiographies. There was, however, more than that; from a different view of life, Barbellion was like Rousseau a truth-seeker, but his portrait of himself was not immutable. It grew clearer as he understood himself better and it changed as he changed; it was not complete when he died at the age of 28, because his own development was not complete.

It is legitimate to wonder to what pitch of excellence he might have brought his Journal, had he lived. In one of his later entries, he says, "Every man has his own icon. * * * A man towards his icon is like the tenderness and secretiveness of a little bird towards its nest, which does not know that you have discovered its heart's treasure. For everyone knows the lineaments of your image and talks about them to everyone else save you, and no one dare refer to his own—it is bad form—so that in spite of the gossip and criticism that swirls around each one's personality, a man remains sound-tight and insulated. * * * Heavens, what a toy shop it will be at the Last Day! when all our little effigies are taken from their cupboards, undraped and ranged along beside us, nude and shivering. For that Day, how few will be able to say that they ever cried, "God be merciful to me a sinner, or a fool or a humbug." The human tragedy begins as soon as one feels how often a man's life is ruined by simple reason of this disparity between the image and the real, the image or the man's mistaken idea of himself like an *ignis fatuus*, leading him through devious paths into the morass of failure, or worse, of sheer, laughing-stock silliness. The moral is: *γνῶθι σεαυτον.* Such a passage enlarges our conception

of the author's capacities and fills in our picture of him. His ill-health and death play the same part in our conception of him that they do in our conception of Keats, with whom, judging by his Journal, he had certain affinities. We do not know what part disease played in conditioning Keats's genius, we only know that it puts a colour into our picture of his life. He does not appear to us as the diseased poet, but as a poet who was stricken with disease. So with Barbellion and Rousseau; they too were in ill-health and write as though they were living a posthumous existence, and in both we find a manifestation of the innermost ruling characteristic which they had in common, the passion of life and for all the sensations life can bring. Whatever may be the theoretical views we hold on the connection between disease and genius, we are able to think less of Rousseau and Barbellion as "cases," but more of them as writers of most illuminating autobiographies which, at least, give us more complete portraits of themselves than that which we can form of Keats from his Odes and his Letters, or of many others from their poems, essays, memoirs and reminiscences.

This leads me to say that the writers of memoirs and reminiscences differ essentially from the autobiographers, because their interest lies in what has come their way and is centred in these other people and things, not in themselves. Just so far as autobiographies depart from the externality of memoirs, they come nearer to the intimate and reflective diaries. These may range from the trivial to the introspective; being immediate they contrast with the autobiographer's narrative of retrospect, but the decisive point is what they have to say. A good example is Pepys because, like both Rousseau and Barbellion, he offers a self-revelation. Pepys has no self outside the thrills of his experiences, because he makes no attempt to separate himself from them; he performs as an automaton, while the other two execute with method, but the result is that through a chaos of the disconnected the man stands unique and is recognized by us all as an artist in life.

Many mental histories, verging on the autobiographic, are full of psychological interest because they reveal processes. Examples of the kind have been given to us by John Stuart Mill, Herbert Spencer, Cardinal Newman and Father Tyrrell. Interesting as indeed is the *Apologia pro vita suâ*, the pages of both Tyrrell and Mill fascinate me more. They present much modesty, which is not an autobiographic characteristic as a rule, also they are alive to the changes and illusions of personality or that tacit effort of our friends to persuade us to be what they think we are, a steady current of suggestion from which, as good autobiographers, they both try to escape. In contrast to these men, there are the autobiographies of the painter, Haydon, and the historian, Gibbon. The former makes us recognize in the struggle of a dreamer with the world a veritable tragedy, while the latter, in his own story, makes us understand how much of the power of his style as a writer is due to the concentrated nature of the man,

that his life-history is really a history of the magnetism of his subject, which he repeatedly refers to as "my Roman decay," that his style was the image of his character and that his art was his nature. It remains only to say that the autobiographer seems rarely to betray as an artist but only as a fallible human being. He generally feels that candour is the essence of his business and it is rare to find the deliberate liar among the self-delineators. From ourselves, all we ask of him is that he shall disclose a personality. The art of interpreting our own lives is not given to many of us, but when it does appear it fixes something which stands above and apart from the banalities of haphazard fiction or the gossip as to manners, customs and all the odd fits of the antique which are the province and stock-in-trade of the annalist. Therein lies the charm of the good autobiography and also of the good letter.

XIII.

L'Académie Française has ruled that our word "gentleman" shall be accepted as a recognized French word. At least, so says my daily paper, and the incident has more than passing interest. I do not propose to discuss who is and who is not a gentleman, as I have already done so elsewhere, but since the same journal persists in always referring to a moving picture hall as a kinema, the inference is permissible that it wishes to return the compliment by incorporating in its daily vocabulary the Gallic version of an imported word. There is, however, a further issue raised and that is, the need for promoting among journalists and others a concern for the purity of the English language. No one will dispute our right in importing, if we cannot coin, words to represent new objects; but it is better that we should adapt and assimilate those words, where we feel so inclined, than that we should merely take them into our tongue and leave them unaltered and looking thoroughly alien, out of mere pedantry. Admittedly, some very useful foreign words do not lend themselves to be anglicized without offending both the eye and ear, notable examples being "shover" for chauffeur and "garridge" for garage. But no man has a right to go about clamouring for "kinema" unless he is also willing to write and say "kykle" or better and perhaps with more reason "kukle" for cycle. The "k," so sedulously cultivated by those who have heard somewhere that the letter "k" like the word kinema or cinema is Hellenic, is a thing we do not want in English unless we feel impelled naturally towards it. We shall not purify English or keep it pure by pedantry of this kind; we shall, in fact, only assist the process of pollution. It may be advantageous to preserve in our spelling of a word some trace of its derivation, but it is against the genius of our language to cling slavishly to any particular foreign consonant.

In critical mood, I am further tempted to say that a general good habit might well have been ruled long ago as to the use of the negatives "un"

or "in" and "less" in our language. The offence is ubiquitous and its correction will be difficult, doubtless, to secure; for who is there who does not give the Teutonic "un" to the Romance or Latin word and even to the Greek, writing "unsymmetrical," "unfortunate" or "ungracious"? Or, who is careful in these days to write "indiscovered" or "inconquerable"? though I believe Bacon was careful to use this latter word. Confusion is everywhere, for we find "incivility" appearing in the same phrase as "uncivil," "ungrateful" with "ingratitude," "undigested" with "indigestible," and "unable" with "inability." The incorrect use of the Teutonic negative particle tacked on to Greek, Latin or Romance words is to be met with everywhere in our literature and yet, on the other hand, the incorrect use of the Latin "in" does not occur. There is nothing that we should prize more dearly than our correct negative particles of both derivations. This is particularly true of the Teutonic derivation in its right Teutonic place, because the "un" implies, denies and refuses so much, as instanced by such words as "undone," "unloved," or "unforgiven." No language but our own has such words of inherent power and strength, but we should try and keep our "un" in its right place and not couple it on to Latin or Greek words. The word "undone" means so much and has the purely English faculty of conveying a depth and sudden greatness of tragedy which is not expressed by saying "ruined" or "defeated." It will be regrettable if the significance and power of the "un" be lost or wasted, but there is a risk of its being wasted if we continue to be so casual and illogical in its use. Let us keep it in its right place. Neither should the less overwhelming "in" be neglected; it is more deliberate and has too its right place and dignity.

Then there is the particle "less" which is used in the most irrational way. I refer to the occasions when it is equivalent to "without" as in "sightless." This particle has a very great value as it locks close meanings with its word, but that word must be a noun and not a verb. It seems unpardonable to meet such words as "tireless," "quenchless," "relentless" and "fadeless." These are not genuine compounds. I can understand the construction of "sightless" because sight is a noun; but what is a "tire," a "quench," a "relent" or a "fade"? By such lapses the words that have "less" for their lawful negative are cheapened and the few laws of grammatical construction for words that we have are violated. It seems to me to be about time we revised our habits and restored to their proper lineage the contemporary histories of our language by a proper distribution of our negative particles "in," "un" or "less." It may be that we are incorrigible and shall never undo our senseless habits. The misfortune is that our incorrect ways were never standardized, or they have standardized themselves by precedent. I admit that, in the present state of affairs, the task of writer or speaker who wishes to behave properly towards his mother tongue is not a happy one. There is no authority to give him advice. I believe there is a Society for the Encouragement of

Pure English but, being neither official nor vested with authority, its doubtless admirable proceedings do not influence either the Press or the Public. There is a British Academy, which is largely a body of scientists with a so-called Academic Committee. It seems to be a pity that an authoritative literary body cannot be evolved from these elements, much on the lines of *L'Académie Française* which has done so much for the French language. We want decisions on many vexed points, and we want an agreed resolve to carry out those decisions. At present the fate of our language is left to anyone who cares to misuse and distort it, with the result that no one thinks the language is improving. As Shakespeare puts it, "Words are grown so false, I am loathe to prove reason with them."

AN ACCOUNT OF SOME OLD BOOKS IN THE COLLEGE LIBRARY.

By Colonel CHARLES H. MELVILLE, C.M.G.
Army Medical Service (Retired Pay).

(*Concluded from p.* 438.)

IV.

SIMPLICIUM / MEDICAMENTORUM / EX NOVO ORBE DELA-/ TORUM, QUORUM IN / MEDICINA USUS / EST, HISTORIA, / Hispanico sermone descripta a D. Nicolaó / MONARDIS, Hispalensi Medico; / Latio deinde donata, & annotationibus, iconibusque / affabre depictis illustrata a CAROLO / CLUSIO Atrebate. / ALTERA EDITIO. / ANTVERPIAE, / Ex officina Christophori Plantini, / Architypographi Regii. / M.D.LXXIX.

Woodcut on title page: hand issuing out of clouds and holding a compass, encircled with a band on which motto, LABORE ET CONSTANTIA is inscribed. Surrounded by a decorative design. On reverse of title page a "Summa Privilegii" in same terms as in case of No. II. Pages numbered to 34. Three pages of index. Bound up with No. II.

The author, Nicolas Monardes, was a native of Seville, and studied Medicine at Alcala de Henarez. He was chiefly a naturalist, and wrote several books. He died in 1578. His publications were:—

De secanda vena in pleuritide, inter Graecos at Arabes concordia Hispal. 1539, 4to. Antwerp, 1564, 8vo.

De Rosa et partibus ejus, Antwerp, 1565, 8vo.

Dos libras de las cosas que se traca de los Indias occidentales, que sirven al usu de Medicina. Seville, 1565, 12mo.; 1569 and 1580, 4to. The edition in 4to. (augmented by a third book), Burgos, 1578; Venice, 1585, 4to. Clusius translated the first two books, Antwerp, 1574 and 1579, in 8vo. Our copy belongs to the second of these editions. The third book was also translatad into Latin by Clusius, Anvers, 1582, 8vo., and into French by Colin, in Lyons, 1619, 8vo.

Libro de dos Medicinas excellentissimas contra todo veneno la Piedra Bezaar y la yerva Escorsonera. Seville, 1580, 8vo.

Libro que trate de la Nieve. Seville, 1591, 8vo. (Praises snow water as a beverage).

Trattato de la Grandeza del Hiero. Seville, 1574, 4to. This book was also translated by Clusius under the title "*Nicolai Monardi Libri tres magna Medicini secreta et varia experimenta continentes.*" Lugdun, 1601, 8vo. (The first book treats of the virtues of bezoar, the second of iron and its properties, and the last of snow and its advantages.)

Del Eseto da varias yervas. Seville 1571, 8vo.

There is also an English translation by John Frampton, in 1577, named "Joyeful newes out of the Newe Founde Worlde." This is believed to contain the first mention in the English language of tobacco.

An account has already been given of Clusius, and of Plantin the publisher, who was a personal friend of both authors, in the notice on No. II.

This book is very much like that already noticed (No. II) but is confined to the New World, whereas Garçia wrote chiefly about the East. The most interesting portion undoubtedly is that which refers to tobacco, for which many therapeutic uses are given. It is recommended as a cure for toothache, and as a preventive of dental sepsis; as a remedy for asthma and persistent cough; for dyspepsia; for worms, both tape and round; for nephritis, for pains in the joints, and as an antidote for arrow poison. On this last point evidence is adduced from its use in the treatment of wounds received during an attack by the Indians, and also from an experiment carried out by the "*Rex ipse Catholicus*" who desiring to test the powers of the drug, ordered a dog to be wounded in the throat. Into the wound some of the poison was first poured, and then some juice of tobacco leaves, in addition a compress of leaves was tied over the wound. "*Liberatus est canis, non sine omnium admiratione.*"

An interesting description is given of its use for the purpose of divination by Indian priests. "It is the habit of the Indians to consult their priests as to the event of war, and other matters of great moment. The priest who is consulted burns a few dried leaves of the plant and takes some of the smoke into his mouth through a cane or tube. He then falls down as if rapt into an ecstacy, bereft of all movement, and thus remains for some time. The effects of the smoke having passed off he returns to himself, and says that he has consulted on the matter with a demon. He then furnishes an ambiguous reply of such a nature, that whatever the event may prove to be, he may easily persuade the people that he had foretold it. In this manner those barbarous men are miserably deceived."

Another use is mentioned. "Our Indians when exhausted with carrying loads or other hard work, inhale the smoke of tobacco, and therewith fall down as if out of their minds; when roused they feel that their powers are recuperated. Negro slaves in imitation of them too often follow their example, from which it follows that their masters beat them severely, and to take away all temptation of an excessive use burn the tobacco."

"The Indians also use tobacco to alleviate thirst and hunger as follows. They burn the shells of shell fish, and pound them like lime. They then mix this with the leaves of tobacco and make a mass of the mixture. From this they roll pills larger than a pea which they dry in the shade. These are set aside for future use. If they have to make a journey through deserts where neither food nor water are to be found they take a store of these pills, and place one between the lower lip and the teeth, sucking the juice assiduously. When one is finished they replace it by

another, and so on till the journey is finished, sometimes for three days, sometimes for four. By this means they say that neither hunger nor thirst trouble them. The cause of this I take to be that the juice of these pills draws down the mucous humours (*humores pituitos*) from the brain, which being swallowed and taken into the stomach, damp down the natural heat, but are eventually consumed by it (the stomach) in the absence of other food, as may be observed in many animals, who remain all winter in their lairs, without any store of nourishment, by reason that their natural heat is preserved by the consumption of their fat, which they have accumulated during the summer."

Monardis concludes his treatise with a letter which he had received from a certain Petrus de Osma, a Spanish officer who apparently had travelled a good deal in Peru, and kept his eyes open. The most interesting part of it is that in which de Osma makes mention of the bezar stone. He says that when on a hunting expedition in the mountains he tried to get information from his natives as to what portion of the particular animal, in which the stone was said to be found, contained it. "They denied, however, any knowledge of the matter (being indeed very unfriendly to us, and loth to impart any of their secrets). An Indian boy, however, of about 10 or 12 years of age, seeing how much interest we had in the matter, showed us inside the animal a small receptacle, or as it were pouch, in which the food is stored, until passed back into the stomach for rumination." Here the stone was found. The other Indians later on got hold of the lad and sacrificed him. De Osma refers to human sacrifice as occurring amongst these people. They appear also to have been addicted to cannibalism, but did not favour Spaniards for this purpose, since their flesh was so hard that it had to be "hung" for three or four days, to render it edible.

V.

PHARMACOLOGIA / SEU / MANUDUCTIO / AD / Materiam MEDICAM IN QUA / Medicamenta Officinalia Simplicia, / HOC EST / Mineralia, Vegetabilia, Animalia earumque / partes in Medicina Officinis usitata, in Methodum / naturalem digesta succincte & / accurate descri- / buntur, / CUM / notis generum Characteristicis, Specie- / rum Synonymis, differentiis & viribus. / Opus omnibus Medicis, Philosophis, / Pharmacopoeis, Chirurgis, & Pharma- / copolis utilissimum.

ὁ βίος βραχύς, ἡ τεχνη μακρη.

Hippocrat., Lib. I, Aphor. 1.

A SAMUELE DALE / LONDINI: / Sumptibus Sam. Smith and Benj. Walford / Societatis Regiae Typographorum, ad insignia / Principis in Coemeterio. D *Pauli.* MDCXCIII.

Carries on fly leaf sanction for publication as follows:—

Hunc librum (cui titulus est / PHARMACOLOGIA) dignum censemus; ut typis / mandetur.

Thomas Burwell, Propraeses
Samuel Collins
Edwardus Hulse
Richardus Morton
Joh. Bateman

Datum 5. Septembris A.D. 1692/in Comitiis Censoribus ex aedibus/Collegii nostri.

Dedication:

CELEBERRIMO/COLLEGIO REGALI/Medicorum Londinensium,/HAEC/NATURAE SPOLIA/ET/ARTIS ORGANA/CONSECRAT/Devotissimus AUTOR.

Preface of five pages; list of abbreviations, two pages; Officina Simplicium, thirty-one pages; Errata, one page; Advertisements, three pages. The body of the work consists of 656 pages, and is followed by four pages of: *Catalogus Librorum Medicorum, qui prostant Venalium apud Sam Smith & Benjamin Walford Londini* 1693.

Bound in leather octavo. Ribbed back; no sign of title label. Lightly tooled boards.

Dale was born, probably, in the parish of St. Mary, Whitechapel, in the year 1659, his father being a "silk-thrower." He was apprenticed to an apothecary, in 1674, for eight years, and subsequently went into practice at Braintree, Essex, where he probably made the acquaintance of John Ray, the well-known naturalist, whose intimate friend and executor he afterwards became. It does not appear that he ever took any medical degree, or became either a member of the Society of Apothecaries, or a Licentiate of the Royal College of Physicians. He died on June 6, 1739, and was buried in the Dissenters' burial ground at Bocking, near Braintree. He was a careful and hardworking botanist, and Ray acknowledged himself as much indebted to him on account of his critical knowledge of plants. Dale's Herbarium is now in the British Museum and exhibits signs of careful and painstaking work.

His chief work was the PHARMACOLOGIA, of which the first edition in 12mo. was published in 1693. The copy in the College Library belongs to this edition. A supplement was produced in 1705, a second edition in 1710, and a third (in folio) in 1737. The British Museum possesses a copy of each edition, but the Physicians' and Surgeons' Libraries have only the later issues. He also wrote an appendix to Silas Taylor's "History and Antiquities of Harwich and Dovercourt" which forms the bulk of the completed work, and gives a full account of the natural history of the district.

That Dale was in a stronger position as a botanist than as a pharmacologist is very evident from a study of his work. As long as he is dealing with the vegetable kingdom he is clearly on his own ground, and writing on a subject with which he is familiar. His descriptions of plants are terse and clear, and yet complete in all necessary detail. Had he been

wise he would have limited himself to writing a herbal. The scheme of his work is however much more ambitious, and he undoubtedly found the labour of completion hard. In his preface he complains, with an obvious reminiscence of Virgil, "*De Ortu & Progressu Simplicium Medicamentorum scribere, majoris molis est, quam Romanam condere gentem*"

He claims to be a follower of Bacon, relying on observation of the processes of Nature, not on imagination and conjecture, and complains not without some justification of the impostors, who through sloth and ignorance have introduced confusion into the Commonwealth of Medicine, preferring rather to err through laziness, and slay pedantically (*otiose errare & erudite necare*) than to work out carefully, and examine, the properties of the drugs in daily use.

It is interesting to note the struggle going on in his mind between the desire to adhere to his principles, and the necessity of saying something about substances of which he is clearly absolutely ignorant, in order to complete the scheme he had laid down for his book.

This is particularly noticeable in the section dealing with precious stones. As regards the diamond he rejects it as a possible test for adultery, and considers that its value in cognate directions is fabulous. When it comes to the question of its administration as a cure for dysentery he evidently prefers to found his objection on its excessive cost, the minimum dose being one drachm.

He is apparently not prepared to deny that the amethyst in two drachm doses can inhibit intoxication, but objects that only a Prince could afford such a prophylactic. On the general question of the use of gems he concludes that even if they do possess some value the same results could be produced from one or other of the commonest herbs.

When again he deals with the animal kingdom he gets very wide of his ideal, and here less excusably. Precious stones, and patients in a position to pay for them, may have been rare in Braintree, but the humbler friends of man were probably easily enough met with. It is, one would think, difficult to support with any actual experimental evidence the exhibition of the louse in jaundice, or the use of earthworms as galactagogues. Doubtless the former, if, as recommended, it is placed inside the *meatus urinarius*, will incite to micturition, and the common bug may have the same power, but the use of spiders and stagbeetles as amulets to ward of paroxysms of intermittent fever, particularly the quartan variety, must one would think have been arrived at by that process "*fingendi aut excogitandi*" which he in his preface so stoutly condemns.

The human body, dead or alive, was also an ample storehouse of remedies. The details are unpleasant; it may suffice to say that without distinction of age, sex, or condition, no portion or secretion of the human body was rejected from use in the treatment of disease.

At the outset, looking back, one is at first disgusted, and later amused by the various *materiae medicae* used, and the virtues ascribed to them.

Later still one sees the justification. There seems to have been two factors at work. One was the realization of the absolute unity of nature. All things, the parts of the body, the various members of the animal and vegetable kingdom, and the various diseases, had certain definite qualities of dryness or humidity, heat or cold, and by means of these any one was able to counteract or supplement the action of any of the others. Thus in one place as an argument in favour of the efficacy of a certain drug in a certain disease it is urged not that it has been tried and found useful, but that because it possesses a certain degree of dryness and heat, it must counteract the action of a certain disease, which has the necessary opposed qualities.

The other factor present was intellectual courage. However much they might boast of their knowledge to impress the vulgar (after all an assumption of infallibility is not unknown amongst successful practitioners at any period of medical history) the best of them realized their ignorance. It was only by working from the widest base that they could possibly arrive at truth: everything had to be tried before the real truth could be attained. Of course we are nearer the truth than they were, since we have had their experience to help us. At the same time if no remedial agents were to be used except those whose intimate reaction on the body could be explained, the professional arsenal would be considerably barer than it is.

Take for instance the use of radium in the removal of tumours. It certainly does seem to remove them, but what difference after all is there (if it comes to a question of actual knowledge of the agent) between wearing one or more radium tubes for cancer, and carrying an amulet to protect one against rheumatism or ague. I have not the slightest doubt that Dale could have produced plenty of cases in which a stagbeetle had been worn as an amulet, and the next paroxysm of quartan fever had failed to appear. His failures he would ignore, as we are all apt to do when we want to prove a particular point.

So I am inclined to be particularly indulgent to our professional ancestors. We shall probably need a good deal of the same indulgence ourselves from our professional offspring, and that is particularly true of those of us who have given hostages to fortune in the shape of books.

Dale mentions in his preface the friends to whom he was chiefly indebted for advice and help, about whom, since a man may be known by the company he keeps, a few words may be not out of place. Of Ray and Hans Sloane it is unnecessary to speak. Martin Lister, who is of the company, came of a well-known medical family, his father, two of his uncles and his son all belonging to the medical profession. I do not know if the greatest holder of the name belonged to the same stock: it would be interesting to know. Lister was a Cambridge man (John's) and became a fellow of his college. He was a naturalist and antiquarian, presenting a considerable number of coins, Roman altars, etc., to the Ashmolean.

He travelled as far as Paris, in the train of the Earl of Portland, in 1698, and his account of the visit (included in Pinkerton's voyages) has a certain historical value. He is also supposed to have been one of the first to suggest the making of geological maps. He was an M.D.Oxford, a Fellow of the Royal College of Physicians, and second Physician-in-Ordinary to Queen Anne. Evidently a man of wide interests and knowledge, on the top of which it is strange to hear that he was a strong conservative in his opinions and a severe critic of Sydenham. He died in 1712.

Samuel Doody was an apothecary in Staffordshire, in succession to his father. Head of the Botanical Garden at Chelsea and a F.R.S. A friend of Ray and Sloane. His attention was directed chiefly to cryptogams.

James Newton lived from 1664 to 1750. He kept a private asylum near the turnpike at Islington, and studied botany to divert his mind from his otherwise depressing occupation. He apparently designed a herbal, but only the engravings, 176 in number, and a list of references is extant.

Tancred Robinson: the longest lived but one of the circle. Born before the Restoration, he saw the Stuarts go, and also the failure of their last serious effort to recover the throne, dying in 1748. Sir Hans Sloane who was born a year or two after him lived five years later. Robinson does not appear to have written any thing beyond occasional papers. No systematic publication is to his credit. He was F.R.S. and Physician-in-Ordinary to George I.

Leonard Plukenet, who is supposed to have been at Westminster under Busby, was an assiduous botanist. His publications contain 2,740 figures of plants with descriptive letterpress. He kept a small herb garden in Old Palace Yard; though a M.D. in practice, it may be conjectured that he spent more time on his plants than his patients.

In fine Dale's friends seem to have been honest hard-working botanists and naturalists, a small constellation revolving round the greater luminaries Ray and Sloane. "Honest hodmen of science" as Huxley described, or is said to have described, Gosse. After all it is greater fame than most of us attain to.

VI.

One hundred and fifty-three / CHYMICAL / APHORISMS / Briefly containing / Whatsoever belongs to the / '*CHYMICAL SCIENCE* / Done by the labour / and study of / '*EREMITA SUBURBANUS* / Printed in *Latin* at *Amsterdam* / *Octob.* 1687 / To which are added / Some other Phylosophic Canons / or Rules pertaining to the / '*HERMETICK SCIENCE* / Made *English* and published for the / sake of the Sedulous Labourers in true / Chymistry; / By *Chr. Packe, Philo-Chymico-Medicus* / *London* printed for the Author, and / are to be sold by *W. Cooper* at the *Pelican* / in *Little Britain*; and *D. Newman* at the / *Kings-arms* in the *Poultry* 1688.

Carries on fly leaf opposite title: [1] *IMPRIMAT.* / Aphorism. Chymic. / *Th. Witherly,* Praeses Coll. / Med. Lond. / *Pe. Barwick* / *Jo. Elliot* / *Rob. Pitt,* / *Joh. Bateman,* / (last four names bracketed) Censores. Two pages of preface addressed "To all the Lovers / of the / CHYMICAL ART," two pages, "the AUTHOR / TO HIS / FRIEND." Text consists of sixty-three pages numbered. On reverse of last, advertisement of "Myographia Nova sive Musculorum omnium (in Corpore Humano hactenus reportorum) accuratissima Descriptio, in sex Praelectiones Distributa, &c., &c. Opera and studio Joannis Browne, Serenissimi Caroli secundi, Brittaniarum Regis, nec—non Nosocomii Regalis, quod est ad D. Thomae, Chirurgi Ordinarii.

The preface by the translator explains how the Chemical Aphorisms came into his hand from Vienna via Antwerp, and when "I had perused them and well weighed them, with what little judgment I could, I thought that I could do nothing more grateful to the Sons of Art, than to publish them in English, which I have done with all the care and exactness I could." After a careful consideration of the matter I have come to the conclusion that the only pertinent part of this preface is the remark about "little judgment." The book indeed appears to be one of the last dying flickers of the Alchemic lamp. It is strange to think that it lasted so long. Yet even Boyle ("Father of Chemistry and Brother to the Earl of Cork") who was certainly a clear thinker had not quite emancipated himself from those superstitions. And he was an old man when this book came out.

The Aphorisms compose a sort of alchemist's litany, consisting of short detached statements as follows:

Aphorism 6. Nevertheless they (the Adepti) have delivered it (Alchemy) but confusedly, enigmatically, and under Allegories.

Aphorism 7. Lest it should fall into the hands of the unworthy.

Aphorism 8. But that it should be known to its own sons only.

Such a method of composition, unless intended to meet the demands of liturgical antiphony, when of course it is reasonable enough, can, one feels, be intended merely to spread a little knowledge over a very wide space. The aphorisms in general consist of a description of the metals, as then known, viz: gold, silver, tin, lead, copper, and iron: their relations to each other, and their composition, as for instance:

Aph. 21. The *Matter* of Metals is either remote or proximate.

Aph. 22. The *Remote* is the Rays of the Sun and Moon, by whose concourse all Natural Compounds are produced.

Aph. 23. The *Proximate* is Sulphur and Argent vive, or the Rayes of the Sun and Moon determined to a Metallic Production, under the form of certain humid, unctious, and viscous Substance.

Aph. 24. In the Union of this Sulphur and Argent vive, consisteth the form of Metals.

The basic idea, and I suppose that there is at least a possibility that

[1] Gothic Type.

we may come back (or go on, is there much difference?) to that sooner or later, is the essential unity of metals, as thus:—

Aph. 60. All the Metals therefore are of the same Original, and arise from the same Principles: and thus naturally to,

Aph. 67. Which transmutation of the imperfect Metals into perfect; that it is not only possible,

Aph. 68. But also true;

Aph. 69. Is confirmed by the common opinion of Philosophers, and by Experience.

The Aphorisms are followed by "Some Phylosophick Rules or Canons, concerning the Stone of Philosophers" 157 in number taken, according to the preface, from *Bernardus G. Penotus a Portu Aquitano*, intended in conjunction with the aforementioned Aphorisms to "together make up a Compendium of the Chymical Art, and may serve the studious for a *vade mecum*, or small pocket Companion, with which he may converse in his retirements." These date back to 1582, and are quite unintelligible to anyone who has not studied Alchemy. Evidently some previous possessor of the book has done so, and found them of value, for here and there paragraphs are marked in the margin as especially valuable. The whole concludes with a few parting words, in that exquisite seventeenth century language, which is almost as impossible to recover in its dignified rhythm and well balanced sentences as the science of alchemy itself.

"Here thou hast (friendly reader) those Phylosophic Canons without which whosoever thou art, thou wilt hardly attain to thy wished-for End. If thou receive these Hermetick Fundamentals with a grateful mind, and exercise thy Self in this Theory with a pious Meditation, time may hereafter bring forth the Praxis of those Rules, not that imperfect or maimed one, which I have shewed to some, but Intire and Compleat confirmed by many Arguments, and solid Reasons. In the mean time, Farewel."

Following on the Canons comes a Postscript to the Reader containing proposals for the publication of all the works of "that indefatigable and highly experienced Chymist, *GLAUBER*, in one entire Folio." Glauber is known to most of us as the originator of an extremely useful laxative, which, under disguise, has probably made the fortunes of many patent medicine men. His activities were much wider, however, and Packe says, "That before his death Glauber was Master of some Phylosophick secrets, I verily believe by his manner of writing; and himself professeth in one of his last Writings, speaking concerning the secret *Fire of Artephius*, That he could now, sitting still in his Chamber, do more with an Egg-shell than heretofore with all his Furnaces and Glasses." This book eventually came out by subscription in 1689.

Christopher Packe himself appears to have been a quack doctor, styling himself a Professor of Chemical Medicine. He does not appear to have possessed any medical qualification, which renders the fact that his book

received the imprimatur of the College of Physicians the more extraordinary. Perhaps it may be accounted for by the fact that he was under the patronage of the Hon. Robert Boyle. He wrote several other books, but they do not bear the stamp of much originality.

In 1674 he published a translation of de Graaf's work, "De Succo Pancreatico" London 12mo. In 1680 Robert Couch's "Praxis Catholica, or The Countryman's Universal Remedy" with additions by himself. London 12mo.

His son, Edmond, took to medicine and seems to have started a family tradition.

The author of the book advertised at the end of the book under notice, "Myographia Nova," &c., was a rather noted surgeon at St. Thomas's; he appears to have been appointed by Charles II (to whom he was Surgeon-in-Ordinary) against the wishes of the governors, in 1683. In 1691 the surgeons revolted against the governors, on the strength of their appointment by royal mandamus; but a new Pharaoh having arisen in 1688, the governors, under Sir Robert Clayton, got their own way, and the surgeons were, it would seem, turned out. In 1698, Browne applied to be restored without success, but was still surgeon to William III, who apparently did not consider that politics need interfere with a man's professional ability. Browne wrote an interesting account of the process of touching for the King's Evil, under the title of *Charisma Basilicon*. He states that 92,107 cases were so treated between 1660 and 1682. Browne, though a Norwich man, and apparently a friend or at least acquaintance of the great Sir Thomas, was no relation of that wonderful writer. He died in 1700.

VII.

HISTORIAR/PLANTA-/RUM. Earum imagines, Nomencla-/turae, Qualitates, & Natale/Solum./Accessere Simpliciu medicamen-/torum facultates, secundum Lo-/cos, & genera ex Dioscoride./Secunda editio.

The whole title page is enclosed in an ornamental classical renaissance border. At foot of page is an oval space in the ornament in which is printed LU-/GDUNI./ Ad Scuti Mediola/Apud Viduam Ga-/brielis Cotery./1567.

Above the word HISTORIA in the title some one has written in MS. in the Greek character "Phytologia," followed underneath by the word "seu." A little lower in red ink "Franciscus B. verus possessor."

The book is 12mo, bound in vellum and in good condition, but looks as if it had been rebound at some date. The pages are numbered to 640, including title page. At the foot of the last is: Historiae Plantarum./ Finis.

Pages, renumbered, 1 to 229. Heading on first page SIMPLICIUM/ MEDICAMENTO-/RUM FACULTATES/secundum locos ex/Dioscoride. There are twenty-five pages of index unnumbered.

The book opens with a preface, GABRIEL COTERIUS LECTORIS, which explains the purpose of the book, which is merely a compilation, giving illustrations of plants with their names in several languages, places

where found, and their virtues. The name of the authority is given in each case. It is in fact what it professes to be, a very handy manual. The plates, of which there are upwards of 638, are very clear and accurate. The English names which are not given in the text have been supplied in MS. in the margin, apparently by Franciscus B., whose name appears on the title page.

The second part of the book, on Simple Medicines, is arranged in sections by diseases or rather symptoms, and parts of the body. Thus the first section refers to the head, and begins with *Ad capitis dolorem ex frigidiate genitum*, which is followed by *Ad Capitis Dolores a calida causa.* Then come the Nerves, Eyes, Ears, Teeth, and so on. On page 133 we get another heading, *Simplicium Medicamentorum facultates secundum genera ex Dioscoride.* This section is arranged under Diseases, beginning with Fevers and going on to Tumors, Wounds, Ulcers and Poisons. Next we have a heading, page 200, *Simplicium Medicamentorum Facultates, quae corpori, decorem praestant, ex Dioscoride.* This begins with baldness, and treats also of depilation, destruction of pediculi, and various unsightly skin affections. Last of all three pages on expulsive drugs for the expulsion of "exuberantes in corpore humores."

Pages 226 and 227 give "Mensurarum et ponderum typi, ad Dioscoridis mentum, Ex Galeno." This gives corresponding values of weights and measures, both liquid and solid.

ON THE EFFECTS OF INJECTIONS OF QUININE INTO THE TISSUES OF MAN AND ANIMALS.[1]

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In December, 1917, Lieutenant-Colonel MacGilchrist of the Indian Medical Service published a paper on the necrosis produced by intramuscular injections of strong solutions of quinine salts.[2] It might be an advantage to quote the first few lines of this communication: "Advocates of intramuscular injections of strong solutions of quinine salts for the treatment of malaria seldom omit to state that no local ill-effects are produced." He records a case of tissue necrosis following on the intramuscular injection of eleven grains of quinine bihydrochloride in thirty-four minims of water. Death supervened thirteen hours later. MacGilchrist especially noted, owing to rapid tissue necrosis, that the track of the needle remained patent. He regards as an established fact that most of the quinine injected is precipitated and probably chemically combined with serum proteins in the necrosed tissues and for this reason intramuscular injections of concentrated solutions of quinine salts are not to be recommended for cases of emergency. Very dilute solutions of quinine salts are, in his opinion, rapidly and completely absorbed, whether employed subcutaneously or by the intramuscular route. If the views which MacGilchrist puts forward in this and other communications are to be accepted without reserve then intramuscular injections of strong solutions of quinine should no longer be employed. It was for this reason that Major-General Sir M. P. C. Holt, K.C.B., K.C.M.G., D.M.S., B.S.F., asked me to carry out an experimental inquiry on animals as to the effects produced by intramuscular injections of strong solutions of quinine.

Human muscle was examined from fatal cases of malaria or suspected malaria which had received an injection of quinine at periods varying from one hour to three months from the time of the inoculation, and in some instances an estimation of quinine in the affected tissues was made. For the experimental inquiry cast mules, rabbits, guinea-pigs and frogs were

[1] This paper was not written with the intention of deprecating the value of intramuscular injections of quinine for the treatment of malaria, but to draw attention to certain facts with which everyone who employs this method should be acquainted. Foreign substances should not be injected into the tissues of man except by those who have the necessary knowledge of the substance they are injecting and the effects it may produce on the tissues.

[2] *Indian Med. Gaz.*, lii., No. 12.

used, while the preparations of quinine employed were (*a*) bihydrochloride in saline, (*b*) acid sulphate in saline,[1] (*c*) quinine alkaloid dissolved in alcohol (about the strength of hospital brandy), (*d*) and in ether (medicinal). The alkaloid shaken in blood serum and saline—a preparation which consisted of one gramme of alkaloid, one cubic centimetre of ninety per cent alcohol, and olive oil to three cubic centimetres—and a somewhat similar preparation to the last mentioned, was tested directly after it arrived in the East for trial. The quinine solutions have been injected in concentrated and dilute solutions. The preparations most commonly employed for intramuscular injections were the bihydrochloride of quinine in saline, and, to a less extent, bihydrochloride dissolved in brandy. Human muscle was obtained in all instances from cases which had received quinine in some form in concentrated solutions as commonly employed for the treatment of malaria. Control observations were made on the action on the tissues of animals of acids and ether (quinine solvents).

Numerous cases were treated with intramuscular injections of quinine bihydrochloride dissolved in brandy on the basis of three grains of the salt per ten pounds of body weight.

Experiments have also been made on the absorption of quinine from the site of inoculation, at periods varying from a few minutes to several weeks, and as to the question of the storage of the alkaloid in the heart-muscle, liver and kidneys.

All who have had experience of malarial patients are aware that an apparent anæmia occurs, and a true anæmia with considerable blood destruction. Further, a severe hæmolytic anæmia and hæmoglobinuria is associated with malaria and may occur at a period of the disease when quinine treatment is essential. For these reasons it was necessary to induce anæmia and hæmoglobinuria in animals by means of immune sera so as to observe whether intramuscular injections of quinine in concentrated and dilute solutions excited a more intense tissue reaction than in the control animals.

All the chemical estimations of residual quinine were undertaken by Captain C. E. C. Ferrey, O.B.E., R.A.M.C. (T.F.), Analytical Chemist to the Central Laboratory, B.S.F., who employed the Stas-Otto process for these investigations.

Quinine and Hæmolysis.

Although the purpose of these experiments was to observe the effects of intramuscular injections of quinine on the tissues, yet attention must be drawn to the hæmolytic activity of quinine as estimated *in vitro*. Two solutions were prepared for the purpose: (1) one per cent bihydrochloride of quinine in saline, (2) a solution of hydrochloric acid in saline of the same

[1] Only three experiments were made with this salt as it was found to excite more intense necrosis than the other preparations which were employed.

total acidity as the quinine solution—0·18 per cent. The total bulk of test solution and saline in each tube was one cubic centimetre. The hæmolytic end point of the quinine solution, acting at 37° C. for five hours, was 0·16 cubic centimetre, while the acid solution alone induced hæmolysis down to 0·1 cubic centimetre. Normal saline was employed throughout the experiments as the diluting agent. Further, the hæmolytic action was much more rapid with the acid solution than with the bihydrochloride of quinine in saline. Normal human serum or citrated plasma in suitable amounts prevented hæmolysis. These results briefly referred to serve to illustrate the hæmolytic action of bihydrochloride of quinine and of the corresponding acid. It will be readily appreciated that the preparations of quinine employed for intramuscular injections in the treatment of malaria are of considerably greater strength than in these experiments on hæmolysis *in vitro*. The hæmolytic activity of a one per cent solution of bi-hydrochloride of quinine is extremely rapid, while strong solutions produce instantaneous hæmolysis. The alkaloid when suspended in saline induces a much more gradual hæmolysis than the salt in solution, although for obvious reasons a considerable error must occur in estimating the hæmolytic action of varying suspensions of quinine alkaloid in saline. It has been found that the agglutination of human or other red cells, well known to be induced by free acids, is absent in the standard acid solutions of bihydrochloride of quinine employed in suitable strengths for such purposes. If 0·05 cubic centimetre of the standard solution of hydrochloric acid already referred to is made up to a total volume of one cubic centimetre, an immediate agglutination occurs on the addition of human red cells, while with 0·15 cubic centimetre of the one per cent solution of bihydrochloride of quinine in one cubic centimetre saline no such effect is induced. All experiments tend to show that although quinine acts as a powerful hæmolytic agent the acid employed to dissolve the alkaloid is much more potent in its effect.

What is the Comparative Effect of Intramuscular Injections of Concentrated and Dilute Solutions of Quinine.

Numerous experiments have been made to solve this question concerning which information was specially required.

The following detailed descriptions express the essential features:—

(1) A rabbit received an intra-muscular injection of 0·039 gramme of bihydrochloride of quinine in 1 cubic centimetre saline, and the same quantity of quinine in 3 cubic centimetres of saline into another set of muscles.

The following day 0·078 gramme of the same preparation in 2 cubic centimetres of saline was injected in the right side and a similar quantity in 4 cubic centimetres of saline in the left.

The post-mortem examination took place on the following day. The results showed that no advantage was gained by injecting the quinine in twice the quantity of saline. The spreading œdema was greater owing to the increase in bulk of fluid injected, while the inflammatory process and muscle necrosis in both instances was so evident that no importance could be attached to minute differences in the affected tissues. If quinine injections are given in such dilutions that the action of quinine and free acids on the red cells and tissues is reduced to a minimum, then the bulk of fluid required would nullify, in my opinion, any advantage that might be gained. Further there is a greater possibility of suppuration from injection of quinine in large bulk into the tissues at frequent intervals.

(2) Four rabbits were injected by the intramuscular route as follows :—

(*a*) 0·018 gramme of bihydrochloride of quinine in 0·5 cubic centimetre saline (concentrated).

(*b*) 0·018 gramme of bihydrochloride of quinine in 0·5 cubic centimetre normal rabbit serum (concentrated).

(*c*) 0·018 gramme of bihydrochloride of quinine made up to two cubic centimetres with auto-rabbit serum.

(*d*) 0·7 cubic centimetre of 1 : 5,000 solution of quinine alkaloid in ether.

(*e*) 0·18 gramme of bihydrochloride of quinine made up to two cubic centimetres with auto-rabbit serum and injected by the intramuscular route.

In every instance obvious necrosis occurred. The interval between the time of the injection and the autopsy was six days in the case of experiments A and B, four days in C and E, and three days in D.

The most intense changes were induced when the alkaloid was injected with ether. Necrosis of muscles in all stages—wide areas of polynuclear and mononuclear inflammation especially towards the capsular area—thrombosis of vessels—red cell agglutination and hæmolytic changes in the tissue blood as well as in the intravascular blood.

(3) A mule was injected with one gramme of alkaloid of quinine in alcohol and olive oil (three cubic centimetres). On the following day with one gramme of the alkaloid in ten cubic centimetres of ether.

Although the total bulk of fluid varied considerably in each inoculation the final results were similar; further, the concentration of quinine in the solutions employed did not affect the final results. In each instance extensive necrosis—hæmorrhage into the tissues—congestion of blood-vessels and foci of acute inflammation were met with. Numerous experiments have been referred to elsewhere in this communication which serve to illustrate the comparative effects of concentrated and dilute solutions when injected into the tissues of animals.

The Microscopical Findings as a Result of Intramuscular Injections of Quinine Salts and Alkaloid Quinine.

The first effect of an injection of a quinine preparation into the tissues is necrosis of muscle. The fibres most affected are completely necrosed, leaving the empty sheaths. Œdema of the tissues accompanies the necrosis, together with agglutination of red cells and hæmolysis in the vessels and in the blood which has escaped into the tissues. These changes are in evidence within ten minutes of the inoculation. At this period no leucocytic reaction has occurred, but an intense congestion of all vessels in the area has taken place. At the end of one hour the leucocytic reaction may not be a marked feature, although in preparations of quinine which include oil an intense polynuclear leucocytic reaction has been observed. The muscle fibres in the necrotic areas, as time advances, present appearances which are various as well as distinctive. In addition to the fibres which are completely necrosed others show fragmentation, so that numerous "apparent droplets" are observed within the sheaths (Pl. I, fig 1). Owing to a multiplication of the nuclei of the sheaths which occurs and a collapse of the sheaths themselves, the fibrous framework of the new tissue is gradually formed. Shrunken fibres with several nuclei give the well-known appearance of pseudo-giant cell formation. The large tissue cells act as phagocytes for fat droplets, red cells and free iron granules. Active destruction of the vessel walls occurs together with thrombosis which may or may not serve as a conservative process (Pl. I, fig. 3). Polynuclear inflammation of the necrosed walls can be clearly demonstrated. Active changes occur in the vessels apart from thrombosis, such as agglutination of red cells and hæmolytic phonemena, while similar changes are met with outside the vessel walls. In certain instances marked red cell agglutination occurs within the vessel without the evidence of inflammation (Pl. I, fig. 2).

In course of time absorption of muscle fragments and of inflammatory products takes place, so that finally we have a condition of fibrous myositis such as is met with as a result of traumatic influence or syphilis. Nerve fibres are implicated in the earliest stages. It is not uncommon to observe that hæmorrhages and large vacuoles occupy the space of the original nerve fibres. Fibrous tissue formation surrounds the nerves in the muscles and also the individual fibres. Large nerve trunks may be so implicated by the œdema and spreading necrosis that complete nerve degeneration occurs.

Strands of necrosed muscle fibres may persist for ten to fourteen days after an injection of quinine, possibly owing to the diminished tissue absorption which must occur as a result of quinine inoculation. The bulk of quinine however is absorbed from the tissues with extreme rapidity—simply a question of hours.

EXPERIMENTS TO ILLUSTRATE THE EFFECTS ON THE TISSUES OF CERTAIN PREPARATIONS OF QUININE.

A cast mule was injected with the following preparations. The results were as follows :—

Number of inoculation	Site of inoculation	Nature of inoculation	Naked-eye appearances at autopsy	Interval between inoculation and examination
1	Back, near side	10 c.c. ether ..	Extensive necrosis, 6 or 7 in. long, 3 to 4 in. wide. Slight superficial œdema	6 days
2	Near fore legs..	,, ,, ..	Extensive tissue necrosis. Slight œdema	5 ,,
3	Back, off side ..	0·25 grm. of alkaloidal quinine in 10 c.c. ether	Widespread œdema. Very extensive necrosis	4 ,,
4	Off fore leg ..	,, ,,	,, ,, ,,	3 ,,
5	Near hind leg..	5 c.c. of 4·3 per cent HCl in saline	Extensive œdema spreading along muscle septa. Marked necrosis	2 ,,
6	Off hind leg ..	5 c.c. of 25 per cent bihydrochloride of quinine in saline (same total acidity as above (5))	,, ,, ,,	24 hours

This experiment gives an excellent survey of the effect produced by ether-quinine alkaloid dissolved in ether—bihydrochloride of quinine in saline—hydrochloric acid made to the same total acidity as the solution of quinine. In Experiment 3 of this series 0·25 gramme of alkaloidal quinine was injected in no less than ten cubic centimetres ether, yet the effect on the tissues was considerable. Here the quinine was given in dilute solution, but the solvent employed was largely responsible for the effect. Experiments 5 and 6 of this series show similar effects on the tissues, yet quinine was not employed in Series 5. The result must have been due, therefore, to the solvent. This fact must never be lost sight of in any discussion on the question of tissue necrosis induced by quinine, as will be referred to elsewhere in this communication.

Intramuscular Injections of Alkaloidal Quinine in Sixty per cent Alcohol.

Several animals received intramuscular injections of quinine dissolved in alcohol, either concentrated or in dilute solutions. The rabbit used in the experiment to be referred to in detail was injected daily for six days with 0·04 gramme in one cubic centimetre of sixty per cent alcohol. Blood counts were made with the object of determining whether a leucocytosis would be induced or an alteration in the red cell-hæmoglobin system. The injections were made in a different muscular area on each occasion. Certain tissues were preserved at the autopsy for quinine estimation, and the entire

local area was removed for a similar purpose except for a small portion reserved for microscopy. First injection: there was marked œdema and a long line of muscle necrosis. A typical fibro-myositis had been produced around the necrosed muscle, in which all possible changes were recognized. Numerous new-formed blood-vessels were present, also blood pigment and scattered hæmorrhages. Degeneration of the vessel walls was evident. The effect of the second inoculation was similar except that a well-developed interstitial neuritis was found in the nerve from the affected area. No quinine was detected in the local lesion. The third injection had produced a large hæmorrhagic area superficial to a diffuse black-brown necrosis of muscle. Numerous foci of polynuclear cells were present. No quinine was obtained from the local lesion. Fourth injection, made four days before death, showed very considerable œdema of muscle and necrosis. Thromboses of some of the large vessels were present with necrosis of the muscular walls. The degenerated muscle fibres were fragmented and were undergoing a process of gradual absorption, by which highly cellular patent sheaths remained, the walls of which ultimately coalesced and thus assisted in the formation of the fibrous scar.

Intramuscular Injections of Quinine Alkaloid in Alcohol.

Dates	Weights grm.	Red cells per c.mm.	H.B. per cent	C.I. (colour-index)	Leucocytes per c.mm.	Differential count of leucocytes—1st column = per cent, 2nd column = number per c.mm.							Quinine alkaloid in 60 per cent alcohol, intramuscular injections, total bulk of fluid = 1 c.c.
						Nucleated red cells, number to per cent leucocytes	Finely granular oxyphil		Lymphocytes		Large hyalines		
							1	2	1	2	1	2	
15.7.18	1,000	5,400,000	83	0·7	8,980	2	43·0	3,827	55·0	4,895	1·5	133	0·04 grm.
15.7.18	950	—	—	—	7,900	1	48·5	3,831	50·0	3,950	1·0	79	0·04 ,,
17.7.18	950	5,200,000	84	0·8	7,600	3	27·5	2,190	38·0	5,168	3·5	266	0·04 ,,
18.7.18	955	—	—	—	7,020	1	32·5	2,275	61·0	4,270	5·5	385	0·04 ,,
19.7.18	1,000	5,200,000	82	0·7	7,100	3	27·5	1,952	65·0	4,615	6·5	461	0·04 ,,
20.7.18	1,000	5,300,000	82	0·7	7,150	—	—	—	—	—	—	—	0·04 ,,
21.7.18	950	5,000,000	80	0·8	6,990	1	27·0	1,863	63·0	4,347	10·0	690	—
22.7.18	923	5,200,000	84	0·8	7,520	0	22·0	1,650	68·0	5,100	8·0	600	Rabbit killed

Fifth injection: Diffuse hæmorrhage and œdema together with a prominent area of greyish brown, dry, muscular necrosis had occurred.

Sixth injection: This was completed forty-eight hours before death. The changes noted at the autopsy were similar to those referred to as a result of the previous inoculation. The microscopical appearances were similar, but of a more acute type. There was a very marked polynuclear inflammation, abundant hæmorrhages, and active hæmolytic changes. The muscle fibres were necrosed, fragmented, and broken up into coarse granules, and hæmorrhages had occurred among the nerve bundles. Both

kidneys and liver removed at the autopsy forty-eight hours after the last intramuscular injection were free from quinine, although 0·24 gramme of alkaloidal quinine had been injected in eight days, and the last injection was only forty-eight hours before death. It will be readily appreciated from those experiments described in detail that alkaloidal quinine given in sixty per cent alcohol excites intense changes in the tissues in the inoculated area.

Injection of Quinine Alkaloid with Olive Oil.

The following preparation was tried for intramuscular injections :—

Quinine alkaloid	1 grm.
Alcohol 90 per cent	1 c.c.
Olive oil (neutral)	to 3 c.c.

Injections were made of 0·2 cubic centimetre of the above mixture into rabbits. Some animals received one injection, others as many as five on successive days. The chief features in such experiments are concentration of the alkaloid and the introduction of a fatty substance on the assumption that it would act as a tissue protector. To avoid needless repetition it will be sufficient to refer to one experiment in detail.

A rabbit received five intramuscular injections of the alkaloid in oil commencing with $\frac{1}{10}$ cubic centimetre containing half a grain of quinine on five successive days. Each inoculation was made into a different area of fresh tissue. The animal was killed eleven days from the first commencement of the experiment. During the period it lost 160 grammes in weight. No advantage would be gained by recording the tissue changes met with in each muscular area. The naked-eye appearances were profound in each focus, as occurs with all concentrated injections of quinine, while the oil exerted no beneficial action. On the other hand an injection of one grain of the alkaloid for a rabbit must be regarded as a full dose. The muscles were soft, showed large areas of necrosis, thrombosis of vessels and hæmorrhages into the muscular tissue. The red hæmorrhagic zone was sharply defined from the necrosed pale area.

Microscopically an extensive fibro-myositis had developed with diffuse muscle necrosis. A polynuclear inflammation was far more in evidence than has occurred in experiments with other preparations of quinine. Nerve fibres embedded in the muscle tissue were degenerated, while in the older lesions fibrous tissue could be recognized among the fibres and surrounding them.

The second injection amounted to one grain of the alkaloid in a total bulk of $\frac{1}{5}$ cubic centimetre. It had the advantage, therefore, for this experiment, of concentration. The inoculation was made in the muscles in the front of the thigh. At the autopsy ten days later it was found that the necrosis had spread to the muscles at the back of the thigh and the great sciatic nerve was surrounded by necrosed and inflammatory tissue. The

nerve was removed entire and sections were prepared in "Marchi" at various levels. An extreme degree of nerve degeneration was noted, in fact, very few of the fibres escaped (Pl. I, fig. 4). Some were completely degenerated, others patchy, while actual hæmorrhages into the nerve had taken place. Here we have an example of the destruction of the sciatic nerve following an injection of quinine. The inoculation was made distant from the nerve, directly into a muscle, and in such a manner that escape of fluid was well-nigh impossible. The necrosis, however, was so excessive that it had extended right through the thigh muscles and implicated the sciatic nerve with disastrous results for the animal. This fact, however, will be referred to later. The entire liver and both kidneys were examined for evidence of quinine storage, but no alkaloid was detected.

The Injection of Quinine Alkaloid in Creosote and Fat.

A preparation which was sent to Macedonia for trial consisting of one gramme of quinine alkaloid, 0·75 cubic centimetre of beechwood creosote and five cubic centimetres of neutral fat, was not found to possess any special advantage over the other preparations referred to. Mules received intramuscular injections of the above preparation, causing extensive necrosis and a gelatinous spreading subcutaneous œdema. A lesion some 6½ inches long, 3 inches deep, and 2½ inches wide was produced by the injection of ten cubic centimetres into the muscle of a mule. Chemical analyses of the necrosed muscle showed that the quinine had been absorbed with rapidity. Two experiments will be quoted to illustrate this point.

	Amount injected	Date	Post-mortem date	Amount of quinine recovered
Expreiment 1 ..	5 c.c. ..	21st ..	25th ..	0·003 grm.
,, 2 ..	5 c.c. ..	22nd ..	25th ..	0·063 ,,

Similar evidence in the case of human muscle was also obtained.

A cast brown horse was inoculated intramuscularly with bihydrochloride of quinine in saline as illustrated in the accompanying table :—

Number of experiment	Amount of bihydrochloride of quinine employed	Interval between inoculation and autopsy	Naked-eye appearance of the tissues at the autopsy
1	2·5 grm. in 5 c.c. saline ..	13 days ..	Marked necrosis and fibrosis
2	1·125 grm. in 2·5 c.c. saline	8 ,, ..	Localized necrosis separated from a fibrous zone by a line of hæmorrhage
3	4·5 grm. in 10 c.c. saline..	3 ,, ..	Long tract of necrosis with marked œdema of muscle
4	2·25 grm. in 5 c.c. saline..	2 ,, ..	Localized necrosis with œdema
5	1·125 grm. in 2·5 c.c. saline	30 hours ..	Very extensive gelatinous œdema with localized necrosis
6	1·125 grm. in 2·5 c c. saline	1¼ ,, ..	Localized necrosis with wide tracts of hæmorrhage

A brief account of the microscopical appearances of the lesions referred to in the previous table will be recorded.

No. 1. Fibrous myositis with complete capsulation of the necrotic muscular tissues. Active polynuclear inflammation present.

No 2. Fibrous myositis completely enclosing necrosed muscle—hæmorrhagic foci and polynuclear inflammation.

No. 3. Extensive necrosis of muscular tissue and of the walls of blood vessels resulting in hæmorrhage and active hæmolytic changes in the diffused blood. Agglutination of red cells very obvious.

No. 5. Wide necrosis of muscular tissue and an intense leucocytic reaction in and around muscular fibres which are fissured, fragmented, and show all stages of degeneration. Active hæmolytic changes and masses of agglutinated red cells present.

No. 6. Diffuse muscle necrosis with long tracts of œdematous tissue evident. Hæmorrhagic foci and active hæmolytic phenomena present. Walls of blood-vessels necrosed and ruptured.

A cast grey mule was injected intramuscularly with certain solutions of quinine with the following results :—

Number of experiment	Amount of quinine injected and total bulk of fluid	Amount obtained at autopsy	Interval between the intramuscular injections and the post-mortem examination	Appearances of the muscle lesions at the autopsy
1	4·1 grm. alkaloid in 10 c.c. of 70 per cent alcohol	0·014 grm.	8 days ..	Fibrosis and extensive necrosis
2	4·5 grm. bihydrochloride in 10 c.c. saline	0·020 ,,	7 ,, ..	Central black necrosis, scattered hæmorrhages. Gelatinous œdema
3	2·25 grm. bihydrochloride in 5 c.c. saline	0·003 ,,	6 ,, ..	Central necrosis with hæmorrhagic zone at periphery. Gelatinous œdema
4	Ditto	0·0085*,,	5 ,, ..	Ditto (Pl. II, fig. 5)
5	1·25 grm. bihydrochloride in 2·5 c.c. saline	0·012 ,,	4 ,, ..	Changes similar, but lesions less extensive
6	4·1 grm. alkaloid in 10 c.c. of 70 per cent alcohol	0·074 ,,	3 ,, ..	Extensive gelatinous œdema surrounding a wide area of dry necrosis (7)
7	2·05 grm. alkaloid in 5 c.c. of 70 per cent alcohol	0·048 ,,	2 ,, ..	Central black necrosis with œdematous tissue around
8	2·25 grm. bihydrochloride in 5 c.c. saline	0·938 ,,	1 hour ..	Extensive dry necrosis about 4 inches square

* This does not represent the sum total because some of the extract was blown out of a flask.

In each instance a different area of the animal's body was used for the injection.

The mule was killed one hour after the last inoculation. At the post-mortem examination the affected tissues in the region of the injections and some of the surrounding healthy tissue were removed for estimation of quinine content, while a small portion was reserved for microscopy.

We can infer from the results of the chemical investigation of the muscle lesions as illustrated in the accompanying table that the bulk of the quinine is absorbed whether injected as an alkaloid in alcohol or as the bihydrochloride in saline. It was also found that at the expiration of one hour from the time of the inoculation to the death of the animal only 0·938 gramme of alkaloid was recovered out of 2·25 grammes injected.

It may be an advantage while referring to the rate of quinine absorption to cite the following experiment.

0·1 gramme of bihydrochloride of quinine in 0·25 cubic centimetre saline was injected into the thigh muscles of both hind legs of a guinea-pig; ten minutes later a similar quantity was inoculated into the muscles of the left fore leg, and the animal was killed immediately. The left hind leg was amputated at the hip-joint and handed to Captain Ferrey entire. He obtained 0·061 gramme of alkaloid from the tissues, which amounts to 0·075 gramme of the bihydrochloride. The tissues in the injected areas showed spreading œdema and marked necrosis of muscle. Agglutination of red cells and hæmolytic changes had occurred. No tissue reaction was present.

The tissues examined *immediately* after the intramuscular injection were œdematous and the muscles showed evidence of necrosis.

Microscopical Changes in the Affected Tissues.

Lesions Nos. 1 *and* 2. The tissue changes in the affected muscles, which are of eight and seven days standing respectively, were similar, although quinine alkaloid was injected in the first case and quinine bihydrochloride in the second. Microscopically there was typical fibrous myositis with diffuse muscle degeneration. The abundance of nuclei in the muscles among the fragmented fibres was very apparent, and in some instances gave the well-known appearances of pseudo-giant cell formation. Large hæmorrhages were observed, more especially in relation to strands of necrosis. Mononuclear cells were numerous throughout the new-formed fibrous tissue, and foci of polynuclear phagocytes. The free iron reaction was demonstrated, and spider cells lying in the fibrous tissue were filled with these granules.

Lesions Nos. 3 *and* 4 resulted from the injection of quinine bihydrochloride on successive days. The fibrous tissue formation was somewhat similar to that which has been referred to in the case of the first two experiments. Large tracts of structureless walls filled with tinged serum were abundant, as also scattered hæmorrhages and phagocytosis of red cells by large mononuclear cells. Necrosis of muscle and splitting up of muscle fibres were more evident than in the first two experiments.

Lesion No. 5. Extensive necrosis of muscle and "vacuolation" had occurred. Some of the larger blood-vessels were thrombosed and complete necrosis of the muscular walls was evident, while other vessels showed

intense polynuclear inflammation. Strands of polynuclear cells were scattered all through the connective tissue stroma.

Lesion No. 6. The most striking feature in this experiment was a zone of necrosed muscle with fibrosis divided from a layer of vacuolated and distorted muscle cells by a broad line of hæmorrhage, while acute œdema extended for some distance between the fibres.

Lesion No. 7. This lesion showed two distinct pathological changes:—

(1) Hæmorrhagic area which contained tracts of free blood and congestion of blood-vessels together with areas of hæmolysed blood in which were present agglutinated red cells. Intense polynuclear inflammation had occurred in the vessel walls and all stages of muscle degeneration.

(2) Necrotic area. The contrast with the vascular area was most marked. Extensive necrosis of muscle with outlying fibres swollen, vacuolated, and distorted, and necrosis of the muscular walls of the large blood-vessels was found. Throughout the whole tissue there was polynuclear inflammation.

Lesion No. 8. This was produced at the end of one hour by one injection of 2·25 grammes of bihydrochloride of quinine. Wide tracts of hæmorrhage occurred along the muscle bundles with acute œdema spreading in all directions. Muscle fibres were necrosed and in all stages of degeneration. In one portion of the affected muscles wide areas of hæmorrhage had occurred with direct destruction of large blood-vessels. In this area intense polynuclear inflammation was present, while in an adjoining area leucocytic reaction was absent. Rings of polynuclear cells were in evidence in the sheath of the muscle fibres, infiltrating the fibres, and dividing them up into large granular masses. Wide areas of lysed and partly lysed red cells were present. Phagocytosis of red blood corpuscles by large mononuclear cells was very evident, also clumps of agglutinated erythrocytes.

Fixation of Quinine in the Tissues.

These experiments were undertaken at the suggestion of Captain J. F. Gaskell, R.A.M.C., so as to ascertain whether quinine when injected into the muscles becomes immediately fixed locally, as if so, quinine "absorption" from the tissues would be only an apparent effect.

Experiment 1. Cast Mule. 1·0 gramme of alkaloid quinine was injected as the bihydrochloride into the belly of a leg muscle which had been exposed for this purpose. The blood-vessels were tied immediately by Captain Moir, A.V.C., and the whole muscle and tendons were removed without delay. The chemical analyses were made by Captain F. S. Hele, M.D., R.A.M.C., and the results were as follows:—

Watery extract, 0·217 gramme.

In muscle, 0·595 gramme.

In cloth (used in the experiment), 0·026 gramme.

Total quantity of quinine alkaloid obtained from the muscle, 0·838 gramme.

Experiment 2: Similar experiment to No. 1 except that the muscle remained in the body for twenty minutes after the blood-vessels were tied by Captain Moir, A.V.C.

Chemical analysis by Captain Hele, R.A.M.C.

Watery extract, 0·307 gramme.

In muscle, 0·460 gramme.

In cloth, 0·029 gramme.

Total quantity of quinine alkaloid extracted from muscle, 0·796 gramme.

The results of these experiments do not suggest that quinine is fixed in the tissues immediately after inoculation to any appreciable extent. Captain Hele considers that the amount "lost" in the above experiments was due to technical difficulties.

The Effects of Intramuscular Injections of Quinine in Animals rendered Anæmic.

These experiments were undertaken to ascertain whether intramuscular injections of quinine produced more severe tissue changes in animals in which a severe hæmolytic anæmia had been induced than in control animals. The anæmia and hæmoglobinuria were induced by injecting rabbits with the serum of a cat which had been immunized with rabbit's cells for the purpose of these experiments. The immune serum was injected intravenously. Blood counts were made at daily intervals and the weights of the animals were carefully recorded. It was necessary to have records of these data because many patients who receive intramuscular injections of quinine are anæmic, and some are suffering from various grades of hæmolytic toxæmia. The most exhaustive experiment will be referred to in detail. Intramuscular injections of bihydrochloride of quinine in saline were given in varying amounts from large to excessive doses with the object of exciting more severe tissue changes in the anæmic animals than in the control. The quinine injections were made previous to and during the period of severe anæmia. There was no leucocytosis. On the contrary, a definite reduction in the total white cells occurred, followed by a rise to the total previous to the inoculation as the condition of the blood improved. A full record of the three most important varieties of white cells is given, but the only noteworthy feature is the absolute increase in larger hyaline cells, as met with in malarial fever. The animal showed the effects of each injection, but no more so than normal rabbits which received similar inoculations. When the animal was killed one month from the commencement of the experiment, the sites of the quinine inoculations were represented as patches of scar tissue which were most obvious in the case of the excessive dose of 0·6 gramme given thirty days before the death of the animal. The results of the microscopical examina-

tion of the scar tissue were similar in each instance. Fibro-myositis—necrosed muscular tissue—scattered round-celled inflammation, well shown as a perivascular effect—and small foci of polynuclear inflammation, were the conspicuous features of the various lesions. To quote this experiment is sufficient for the purpose intended, as it is definitely shown that quinine when given by the intramuscular route in concentrated and massive doses

Dates	Weights grm.	Red cells per c.mm.	H.B. per cent	C.I. (colour-index)	Leucocytes per c.mm.	Differential count of leucocytes—1st column = per cent, 2nd column = number per c.mm.							Doses of quinine bihydrochloride in saline, total bulk injected on each occasion = 1 c.c.
						Nucleated red cells, number per cent of leucocytes	Finely granular oxyphil 1	2	Lympho-cytes 1	2	Large hyaline 1	2	
29.5.18	1,510	6,000,000	100	0·8	7,500	0	21·9	1,642	76·0	5,700	0	0	—
30.5.18	1,490	—	—	—	—	—	—	—	—	—	—	—	0·25 grm.
31.5.18	1,490	—	—	—	—	—	—	—	—	—	—	—	0·45 ,,
1.6.18	1,510	6,000,000	100	0·8	6,400	0	32·6	2,086	66·0	4,224	0·6	38	0·6 ,,
2.6.18	1,515	—	88	—	—	0	13·0	—	85·3	—	1·0	—	0·45 ,,
3.6.18	1,445	4,300,000	50	0·5	7,200	6·0	20·0	1,440	79·3	5,709	0	0	—
4.6.18	1,400	1,500,000	32	1·0	5,000	7·0	27·0	1,350	72·3	3,615	0·6	30	0·09 grm.
5.6.18	1,400	1,500,000	32	1·0	4,500	2·0	34·0	1,530	65·3	2,938	0	0	—
6.6.18	1,390	2,000,000	36	0·9	5,200	1·0	55·0	2,860	44·6	2,319	0	0	0·045 grm.
7.6.18	1,300	2,056,250	40	1·0	5,400	4·0	34·3	1,812	56·6	3,056	4·3	232	—
8.6.18	1,330	2,170,000	35	0·8	5,000	16·5	60·0	3,000	40·0	2,000	0	0	0·15 grm.
9.6.18	1,335	3,280,000	65	1·0	4,900	10·0	30·0	1,470	69·0	3,381	1·0	49	—
10.6.18	1,365	3,290,000	65	0·9	6,800	2·5	32·0	2,176	67·5	4.590	0·5	34	—
11.6.18	1,320	4,200,000	66	0·7	7,260	2·0	42·0	3,024	55·0	3,960	2·0	144	—
12.6.18	1,350	4,290,000	65	0·7	7,280	2·0	29·0	1,988	66·0	4,756	5·0	360	—
30.6.18	1,610	4,496,875	82	0·9	7,220	0	31·0	1,532	58·0	4,176	9·0	648	—

excites no greater reaction in the tissue of animals rendered anæmic than in the case of the normal, while no general effect occurred even when the inoculations were made on successive days. Other experiments completed on these lines led to similar conclusions. One rabbit, in which a severe experimental anæmia had been induced, received two massive intramuscular doses of quinine during the period of hæmoglobinuria, but the effects were similar to those obtained in the control animals, while a diminution in the total leucocytes was recorded.

Human Muscle.

Muscle tissue from the region of a previous quinine inoculation has been examined from several cases in the Command. The interval between the inoculation and the examination varied from so short a period as one hour up to three months. It has been suggested that the effects of quinine on the tissues is not capable of demonstration until twenty-four hours from the time of the inoculation. This view is erroneous on experimental

evidence while it is equally fallacious in the case of a human subject. A man, comatose from malarial fever, was admitted to hospital, an intramuscular injection of twenty grains of bihydrochloride of quinine was given, but the patient died one hour later. At the autopsy a large area of black-green necrosis, about four by four inches, surrounded by gelatinous œdema was discovered at the site of inoculation. All cases which I have had the opportunity to examine have received concentrated quinine. Experimentally, quinine injections can be given and the autopsy performed immediately, but the necrotic action is quite obvious. No detailed description of the microscopical changes will be given in this section except such as refer to points of special importance. Certain cases of special interest will be briefly referred to so as to illustrate the most essential features as regards quinine inoculation. Twelve grains of bi-hydrochloride of quinine were injected into the right buttock forty-eight hours before death. At the autopsy a large area of complete necrosis of muscle was observed together with a wide tract of hæmorrhage due, as was proved on microscopical examination, to complete destruction of the wall of a large artery. The entire necrosed muscular tissue, together with that tissue in immediate contact, was examined chemically, except for a small portion reserved for microscopy, but no quinine was detected. Two intramuscular injections of fifteen and twenty grains respectively had been made at an interval of twenty-four hours and death occurred about twenty hours later. The resulting lesion was similar in each case—large area of necrosis, a band of hæmorrhage and congestion, with a wide tract of gelatinous œdema.

In the case of a Greek labourer who had received an intramuscular injection of fifteen grains of bihydrochloride of quinine twenty-two hours before death, only 0·02 gramme of the alkaloid was obtained from a large area of necrosis at the seat of the inoculation. The absorption here was rapid in spite of the fact that the patient was dying from fulminating pneumococcal septicæmia.

Certain cases of malarial fever with malarial parasites present in the circulating blood were complicated with blackwater fever, but the effects from intramuscular injections of bihydrochloride of quinine were similar to those observed in the uncomplicated cases, except that the hæmorrhagic zone appeared darker in colour, almost black in some instances (Pl. II, fig. 6).

One of the most important cases which illustrate the action of quinine occurred in the case of a man who died from blackwater fever and malaria. Four days before death he received an intramuscular injection of twenty grains of bihydrochloride of quinine. The inoculation was made into the same buttock which had been injected three months previously with a similar dose for malarial fever. This man had complained of aching and cramping pains in the buttock at the site of the inoculation, especially if he sat for any length of time on a hard seat or had prolonged exercise. At the autopsy intense necrosis had occurred at the site of the recent injection

which merged into the old lesion, which showed dense fibrous tissue at the centre of the focus, and a definite broad band of fibrous myositis at the periphery. Acute polynuclear inflammation from the recent injection had extended to this layer of fibrous myositis. The pain referred to could be explained by the patch of dense fibrous tissue in the centre of an important muscle surrounded by a zone of fibrous myositis, but further, owing to a fibro-neuritis which existed in this area. Some of the nerves of the muscle were surrounded by dense fibrous tissue, and similar foreign tissue had replaced many of the nerve fibres. Similar examples were met with in cases of much shorter duration, and also experimentally, a fibro-myositis, and fibro-neuritis.

A patient was admitted to hospital with malignant malaria. He received an intramuscular injection of 1·33 grammes of bihydrochloride of quinine but died two hours later. The whole of the necrotic tissue, which was three inches square, surrounded by œdema, was removed for chemical investigation, except for a small portion reserved for microscopy. There was extensive necrosis of muscle, necrosis of the walls of blood-vessels, marked evidence of hæmolysis, but no acute inflammation was present.

Although the patient was inoculated when *in extremis*, only 0·344 gramme of alkaloidal quinine was extracted from the tissues.

The fact that necrosis of the tissues always accompanies the intramuscular or subcutaneous injections of quinine is not realized sufficiently by medical officers, even those who have employed these methods on a large scale. No better illustration of the correctness of this statement can be furnished than by quoting the following instance. Owing to certain bad results which had occurred from intramuscular injections of quinine, an Army order was issued to the effect that all divisional officers must report in detail to the D.M.S. any ill effects subsequent to intramuscular injections of quinine. One divisional officer after fifteen months' experience of this method of treatment of malaria furnished a report to the D.M.S. to the effect that a man had died from malaria and at the post-mortem examination a wide area of necrosis of muscle was found at the site of injection. He concluded his evidence with the statement that all medical officers in his unit had been warned of this unfortunate incident and that every effort would be made to prevent a recurrence of this disaster! I have discussed the question of quinine necrosis with innumerable medical officers who have had wide experience of intramuscular injections of quinine and it is by no means uncommon to learn from them that they were unaware that such effects occurred in the tissues apart from negligence. It is this lack of knowledge of the methods of quinine administration which serves to explain the cause of many of the disasters which have occurred. It is, therefore, necessary to emphasize that quinine injections should not be given in the vicinity of large nerve trunks, or main arteries, that the injections should not be repeated in the same area of muscular tissue, and that

this method of quinine administration should only be employed when circumstances demand it.[1]

The chief complications of intramuscular injections of quinine in the human subject during 1916-17 and 1918 of which I have records were as follows: (1) Tetanus, (2) Gangrene, (3) Abscess formation, (4) Pyæmia, (5) Nerve palsies, (6) Hæmorrhage from large arteries, (7) Sciatica, (8) Chronic muscular pain, (9) Pain and deficient movements in affected muscles, (10) Thrombosis in varicose veins.

The Results of the Estimation of Quinine Alkaloid in Human Muscle subsequent to Quinine Injections.

No. 1, broncho-pneumonia. Intramuscular injections of twenty-one grains of bihydrochloride of quinine into left buttock. Two days later twenty-six grains were injected on the opposite side. Death on the following day. Amount of quinine alkaloid recovered from first injection, 0·227 gramme, and from the second injection, 0·345 gramme.

No. 2, malignant malaria. Intramuscular injection of fifteen grains of bihydrochloride of quinine. Death four days later. Amount of quinine alkaloid recovered, 0·002 gramme. This patient had received ten intramuscular injections in fourteen days amounting to 115 grains, and six intravenous injections which totalled fifty-five grains.

No. 3, malignant malaria. Intramuscular injection of ten grains of bihydrochloride of quinine. Death three days later. Amount of quinine alkaloid recovered from muscle, 0·0115 gramme.

No. 4, lobar pneumonia. Intramuscular injection of fifteen grains of bihydrochloride of quinine. Death twenty-four hours later. Amount of quinine alkaloid recovered from muscle, 0·048 gramme.

No. 5, malignant malaria. Intramuscular injection of eighteen grains of sulphate of quinine. Ten days later large quantity of pus evacuated. From fifty cubic centimetres of the pus, 0·0012 gramme of quinine alkaloid was obtained.

No. 6, malignant malaria. Intramuscular injection of ten grains of bihydrochloride of quinine. Death twenty-six hours later. Amount of quinine alkaloid recovered from muscle, 0·041 gramme.

No. 7, malignant malaria. Intra-muscular injection of twenty grains of bihydrochloride of quinine. Death two hours later. Amount of quinine alkaloid recovered from muscle, 0·344 gramme.

No. 8, lobar pneumonia, pneumococcal meningitis. Intramuscular injection of fifteen grains of bihydrochloride of quinine. Death twenty hours later. Amount of quinine alkaloid recovered from muscles, 0·0215 gramme.

In every instance the quinine was injected into the muscles in concen-

[1] The oral method of administration of quinine is greatly neglected by some medical officers who are placed in charge of cases of malarial fever.

trated solution—the total quantity of fluid injected did not amount to more than a few cubic centimetres. The results show, however, that the absorption was rapid, as only traces of quinine were recovered from the entire lesions, apart from a small focus which was reserved for microscopy, and from the surrounding muscular tissue. In No. 7, twenty grains of the bihydrochloride of quinine were injected into the muscles, and the patient died two hours later, but only 0·3 gramme was recovered. In each instance the area of necrosis was considerable, and the tissues showed very marked changes on microscopical examination.

An Examination of Muscle Tissue necrosed from Quinine Injections for the Presence of Malarial Parasites.

Certain specimens of muscular tissue which had been examined for the presence of malarial parasites subsequent to the injections of quinine showed most unexpected results. The blood cells in the necrotic vessels were completely hæmolysed, yet malarial parasites were present in some instances in relatively large numbers and the bodies of the parasites were well stained. The parasites would be diminished in numbers as compared with the control muscle from another area of the body or from some visceral lesions, but perfectly staining parasites were found lying in a necrosed vessel in which there were no normal red cells. It is strong evidence that destruction of red cells and tissues generally is much more readily excited by quinine solutions than destruction of malarial parasites:—

One case will be referred to in detail to emphasize this fact:—

Malignant Malaria.—Blood film showed a very heavy infection of red cells with the ring form of parasites. Sporulating parasites were also numerous. Time 10.30 a.m.

Twenty grains of bihydrochloride of quinine were injected intramuscularly at 11 a.m., and twenty grains were injected intravenously. Death at 3.45 p.m. on same day.

Wide areas of necrosis of muscle at the seat of the quinine injection existed. There was great destruction of the walls of blood vessels and the blood cells were completely lysed, while the muscle tissue itself showed considerable necrosis. Large dot parasites with well-stained bodies and abundance of pigment were relatively numerous lying among the red cell debris. Parasites however were far more numerous in the internal organs and in other muscular areas.

Intramuscular Injection into Frogs.

Several frogs received intramuscular injections of quinine bihydrochloride in saline in suitable doses for body weight, and were killed three hours later. The muscles at the sites of the quinine injections were opaque. There was marked œdema, complete necrosis of muscle fibres,

other fibres vacuolated or represented as granular masses and hæmolysis of red cells in the affected areas.

Four frogs with an average weight of sixty grammes were injected (I.M.) with quinine and the resulting lesions were as follows:—

(1) Frog injected with 0·0004 gramme of quinine bihydrochloride (0·1 cubic centimetre) and killed twenty-two hours later. Muscles opaque and showed extensive necrosis.

(2) Frog injected with 0·0004 gramme of alkaloid in 0·02 cubic centimetre of ether and killed twenty-two hours later. Extensive muscular necrosis. Slight inflammatory reaction.

(3) Quinine injection as in case of frog 1. Animal killed three days later. Extensive muscular necrosis—abundant hæmorrhages—and widespread inflammation were very evident.

(4) Frog injected with 0·0004 gramme of the alkaloid suspended in saline and killed three days later. Results similar to Experiment 3.

These results were similar to those obtained in the case of the warm-blooded animals.

Conclusions.

(1) Concentrated preparations of quinine produce more intense necrosis than dilute, but dilute preparations such as are of practical utility excite œdema and necrosis at the site of inoculation. The differences between these two methods of quinine inoculation is not of sufficient value to justify active opposition to the method commonly employed.

Inoculation of quinine in solutions so dilute as to avoid œdema and tissue necrosis is not of practical utility in the human subject.

(2) A concentrated solution of quinine is absorbed rapidly from the tissues as shown by chemical analysis, even in patients who are *in extremis*. It is not apparently stored as such in liver, kidneys, or heart muscle.

(3) It is essential to realize that tissue necrosis—spreading œdema and local blood destruction—are produced by the solvents employed for quinine administration and the effects are only slightly inferior to those excited by quinine salts and the alkaloid.

(4) No advantage was obtained by the addition of olive oil or fat or by injecting the alkaloid dissolved in alcohol, or ether, whether in concentrated or in a dilute solution.

(5) Tissue necrosis occurs immediately and persists for a considerable period. In some instances the fibro-myositis which results is associated with a fibro-neuritis which causes various symptoms definitely related to the pathological processes.

(6) Necrosis of blood-vessels in the area of inoculation is a common result. This leads to small hæmorrhages into the tissues, and has caused severe hæmorrhages in the human subject, and experimentally, from

rupture of a large vessel. The destruction of the vessel wall is associated with an accompanying thrombosis.

(7) An extensive necrosis produced by an intramuscular injection of quinine in the neighbourhood of an important nerve trunk, may result in nerve palsy. Experimentally, complete degeneration of the great sciatic and other nerves has been produced apart from any direct injury to the nerve at the time of the inoculation. In the human subject this disastrous result may be due to spreading œdema and extensive tissue necrosis.

(8) Experimentally, no leucocytosis has ever occurred from quinine injections; on the other hand a leucopenia may develop, while an increase of large hyaline cells has been recorded on several occasions.

(9) No essential differences in the degree of tissue necrosis from intramuscular injections of quinine in malarial fever or malarial fever associated with blackwater fever were observed.

(10) Repeated intramuscular injections of quinine should not be given into the same area of muscle, or tissue directly adjacent, as otherwise permanent injury of muscle [1] or nerves may occur.

ACKNOWLEDGMENTS.

To Captain C. E. C. Ferrey, O.B.E., R.A.M.C. (T.F.), Analytical Chemist to the Central Laboratory of the B.S.F., I am greatly indebted for the whole of the chemical analysis of the tissues for the determination of the presence and amount of quinine. This investigation, which has been a laborious process, is of the utmost value in association with the histological findings.

To Captain Moir, A.V.C., Bacteriologist to the A.V.C., B.S.A., I am indebted for considerable help in the investigation of the cast mules and horses which were inoculated with quinine.

Captain A. Wilkin, R.A.M.C., rendered me valuable assistance during the process of the work.

The tissue from human sources has been procured for me by various bacteriologists in the command, to whom my thanks are due.

To Cpl. P. Panichelli, M.S.M., R.A.M.C. (T.F.), I am indebted for the illustrations which serve to explain what the text is incapable of defining.

[1] The gluteal regions, obtained from a man who had daily intramuscular injections of quinine, nine in all, were shown at the British Medical Association meeting in London, 1919. As a result of the injections wide tracts of muscle were necrosed and only fragments of healthy tissue remained.

PLATE I.

FIG. 1.

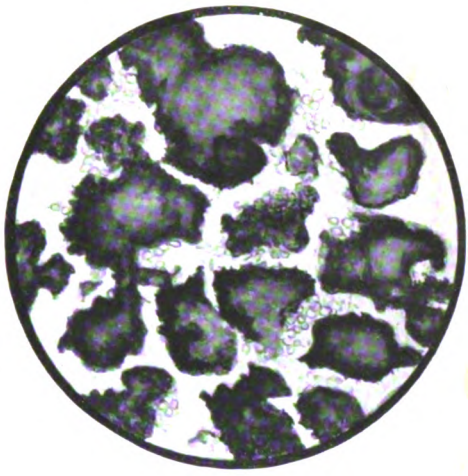


FIG. 2.

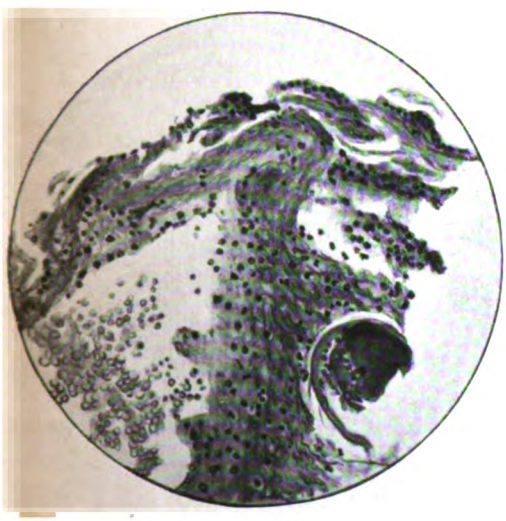


FIG. 3.

FIG. 4.

To illustrate "On the Effects of Injections of Quinine into the Tissues of Man and Animals," by LEONARD S. DUDGEON, C.M G., C.B.E., F.R.C.P.Lond.

PLATE II.

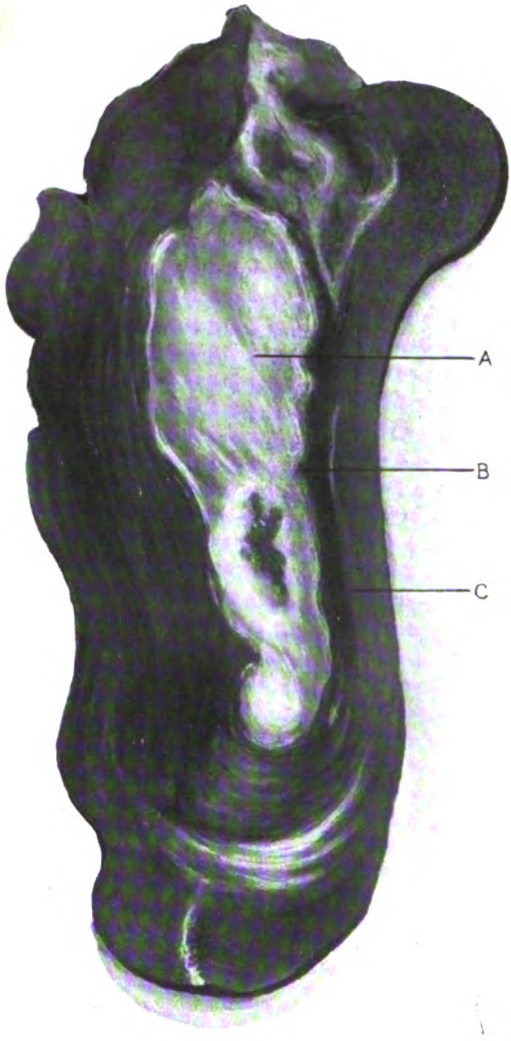


FIG. 5.

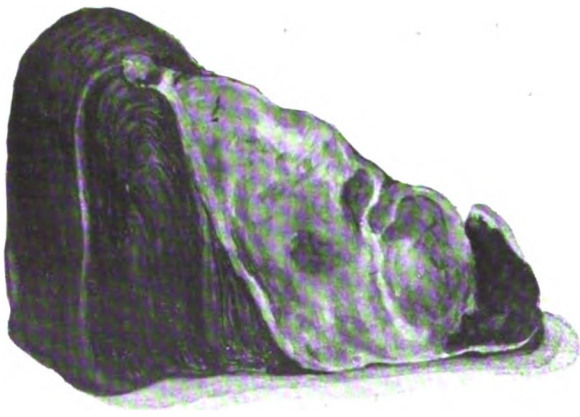


FIG. 6.

DESCRIPTION OF PLATES I AND II.

FIG. 1.—*Quinine rabbit*, 53-(4). Section of muscle from a rabbit which had received an intramuscular injection of 0·04 gramme of alkaloid quinine in one cubic centimetre of alcohol four days before death.

FIG. 2.—Agglutination of red blood corpuscles in a large vessel in the tissue of a horse which had been injected with 1·1 grammes of bihydrochloride of quinine thirty hours previously.

FIG. 3.—Complete necrosis of large artery as a result of an intramuscular injection of quinine alkaloid in brandy.

FIG. 4.—Section of great sciatic nerve in a rabbit which had received an intramuscular injection of 1 grain of quinine alkaloid in alcohol eleven days previously.

FIG. 5.—Muscle from a mule which had received 2·25 grammes of bihydrochloride of quinine in five cubic centimetres of saline five days before death. Natural size. A. Œdema, necrosis, patches of hæmorrhage. B. Hæmorrhagic line showing intense inflammation. C. Œdematous muscle.

FIG. 6.—Portion of human muscle from a case of blackwater fever and malaria. Patient had received an intramuscular injection of 20 grains of bihydrochloride of quinine forty-eight hours before death. Natural size.

Clinical and other Notes.

NOTES ON THREE CASES OF ALASTRIM.

By Lieutenant-Colonel G. M. GOLDSMITH, C.B.E.
Royal Army Medical Corps.
AND
Major W. F. M. LOUGHNAN, M.C.
Royal Army Medical Corps.

The following notes on this unusual disease may be of interest:—

Case 1.—Private "S." was admitted to hospital on May 25 complaining of severe headache, and slight pain in the lumbar region, temperature 103° F., pulse 84. He stated he had not felt well for two days previous to his admission to hospital. On examination a few papules were present over both sterno-mastoid regions of the neck, and also on the back of the wrists. The skin on the rest of the body presented nothing abnormal. The tongue was thickly coated and the bowels were constipated. The patient had been vaccinated three years ago, and bore good vaccinia marks. May 26, 1920: The neck, upper part of the back and the forearms up to the elbow were covered with small discrete papules, showing no inflammatory zone. Temperature 102° F. Pulse 80. The majority of the papules of May 25 had become vesicular, and were somewhat irregular in size, with a marked tendency to become confluent. 27th: A crop of vesicles appeared all over the body, including the scalp, the greater number becoming confluent on the buttocks and gluteal regions. The soles of the feet and palms of the hands were free from any signs of the eruption. 29th: The earliest papules had now passed through the vesicular stage and had become somewhat contracted, dark and pustular. June 1: The body was now covered with pustules, a few papules and vesicles still remaining on the chest and upper part of the back. Temperature 99° F. Pulse 88. 3rd: The skin was covered throughout with pustules, a few vesicles were still present about the neck. Temperature 99·6° F. Pulse 86. Bowels only moved with aperients, tongue coated, appetite very good, patient stated he felt very well, 5th: Some of the pustules have become smaller and darker, and a few show early scab formation, particularly on the chest, back and buttocks. Temperature 99·8° F. Pulse 88. 7th: Many of the pustules on the chest, back and buttocks have become dark and dry, but no signs of umbilication are demonstrable. Temperature 98·6° F. Pulse 74. 9th: The cutaneous system shows but a few pustules, and is covered with small discrete scab formations, many of which have become confluent on the buttocks and gluteal regions. Temperature and pulse normal. 12th: The scabs remain, but a few have fallen off about the chest, leaving a dark zone but no marked scarring. The patient feels perfectly well, his tongue is clean, bowels acting normally, appetite good, temperature and pulse normal. 15th: Most of the scabs on the chest, back and buttocks have dropped off, leaving practically no scar formation. 17th: The skin is almost clear of any scab formations, with the exception of the axillary regions where a few

scabs still remain. 20th : The skin is clear of all scabs, and shows a slight reddish mottling, without scar formation.

Case 2.—Private " W " was admitted to hospital on July 26, 1920, complaining of " fever " and pain in the back. On examination the neck was covered with small raised papules, which could not be seen on any other part of the body. The tongue was furred, and the bowels had not moved for two days ; a few papules were present on the buccal mucous membrane. Temperature 102·5° F. Pulse 90. Patient stated that he felt weak, and could not take his food for the three days previous to coming to hospital. He had been successfully vaccinated eighteen months ago. July 27 : Most of the papules on the neck had become clear and vesicular, a number of new papules appeared on the chest and back. Temperature 100° F. Pulse 86. The palms of the hands and the soles of the feet were free from any signs of eruption. 28th : No new papules have appeared on the body, the old ones have almost all become vesicular. 29th : The vesicles are still present but slightly enlarged and darker in colour : no further appearance of any fresh vesicles can be seen. 31st : Many of the vesicles have become yellow and pustular. Temperature 99·8° F. Pulse 90. August 2 : Most of the vesicles have passed into the pustular stage, a few vesicles still remaining about the axillary folds. Temperature 100·2° F. Pulse 96. 4th : Many of the pustules have become contracted and appear to be drying. 5th : The majority of the pustules show signs of scab formation. 7th : Drying of the pustules and scab formations present throughout the whole cutaneous system. 10th : Many of the scabs on the neck have dropped off, leaving small reddish zones, but no scar formation. 14th : The scabs have completely disappeared leaving a reddish mottling. Patient states he feels perfectly well. This patient was re-vaccinated during the attack and completely failed to take.

Case 3.—Private " L " was admitted to hospital on July 31, 1920, complaining of severe headache, sore throat, loss of appetite, furred tongue and constipation. On examination the tonsils appeared to be hyperæmic. The cutaneous system showed a few papules over the region of the manubrium sternum, and on the anterior surface of the elbow joints. Patient was successfully vaccinated one year ago. August 2, 1920 : The chest and upper part of the back are covered with papules. Temperature 99·8° F. Pulse 88. 4th : Several vesicles present over the clavicular and sternal regions, and over the upper part of the back. 5th : Almost all the papules have become vesicles, and a few of the vesicles about the root of the neck show signs of early pus formation. 8th : Nearly all the vesicles have become pustular. Temperature 100·4° F. Pulse 98. 10th : Many of the pustules have become dry, and somewhat raised, but no umbilication or itching is present. 13th : The great majority of the pustules have undergone scab formation, a few still remaining in the pustular stage in the axillary regions. 16th : All the pustules have disappeared, nothing but dried scabs are to be seen, many of which have dropped off. 20th : Many of the scabs have dropped off, leaving small raised hyperæmic areas, but no scarring or loss of tissue is to be seen. 24th : The scabs have completely disappeared, and the patient states he feels perfectly well. This patient was vaccinated during the attack, but completely failed to take.

The cases of which the above notes are given occurred in Jamaica, where an epidemic now prevails amongst the civil population. The disease has many

synonyms and is often spoken of as *Amaas or Kaffir milk-pox in South Africa.* It is an acute specific exanthema bearing a close resemblance to smallpox in its clinical signs, but its symptoms are much milder, *and it might be considered to occupy middle place between variola and varicella.*

One of the earliest accounts of the disease was given by Anderson, of an epidemic that occured in Jamaica in 1866. *Lasselle and Dickson described a similar outbreak in* 1903. Scheult has described the disease as occurring in Trinidad in 1903 and 1904. It has also been reported from South America and South Africa.

The etiology of the disease is u nknown, *and vaccination against smallpox does not seem to be protective against alastrim.* The point to be settled is whether it is a true smallpox, a smallpox modified by vaccinal immunity, a varicella or a new disease.

Alastrim differs from smallpox in the following points :—

(*a*) Vaccination against smallpox affords but slight protection from alastrim. The disease can occur after recent successful vaccination.

(*b*) The severe lumbar pain of smallpox is absent in alastrim.

(*c*) The secondary fever during the pustular period is very mild, and may be absent in alastrim.

(*d*) True umbilication of the scabs is not seen.

(*e*) The very mild form it takes in adolescents.

(*f*) Absence of scar formation.

(*g*) Low mortality rate—1·5 to 2 per cent.

Alastrim differs from chicken-pox in the following points :—

(*a*) It occurs at all ages.

(*b*) The marked tendency of the vesicles to become confluent.

(*c*) The disease is liable to be prolonged in all its stages, and more particularly in the pustular stage, which may last as long as ten days.

The symptoms consist of headache, furred tongue, constipation, mild lumbar pain, fever and increased pulse rate. The papules appear when the temperature falls about the third day ; when the appetite returns and the patient feels much better. Secondary fever during the pustular stage may be present from the eighth to the tenth day, but it may be mild or absent altogether. The rash is not seen on the palms of the hands or the soles of the feet, but it may be present all over the body including the scalp. Itching and glandular enlargement do not seem to occur.

THE FIELD AMBULANCE AND ITS ORGANIZATION.

By Lieutenant-Colonel WALTER L. WATT, M.D.
Canadian Army Medical Corps.
Officer Commanding Granville Canadian Special Hospital.

A field ambulance, as a unit, should be characterized by :—

First, Elasticity.—The number of wounded and sick it may be required to look after varies from zero to infinity. It is only supposed to be equipped for 150 patients, but in times of stress this number will be multiplied many times over, our highest number of admissions being 1,250 in twenty-four hours.

Second, Harmony.—There must be no working at cross purposes. Every officer and every man must have his own particular work to do, and there should be no interference whatever with such duties.

Third, Inter-co-ordination.—Each section should not only be fully qualified to relieve any other, at any time, and at any work, but within itself each half-tent or half-bearer sub-division should likewise be able to relieve the other, no matter what the work may be.

Fourth, Efficiency.—It is taken for granted that the officers are fully qualified in their profession, but there is no one more hopeless in a field ambulance than an officer who is purely a physician. The work of a field ambulance depends entirely on the military efficiency of the personnel, the rapidity with which the bearers collect, load and unload patients, with which the tent orderlies prepare the wounded for the hands of the surgeon, the celerity of the orderlies in bandaging and assisting when the great rush is on, the organized marshalling of ambulances pouring in and out with their loads of wounded, the proper and careful checking of patients, the systematic feeding of the wounded, many of whom have not tasted food for twenty-four to forty-eight hours. These are all factors in determining the wastage in output of work for the energy expended.

Fifth, Foresight.—Trouble comes like a thunderstorm on the clearest of days. Only a few minutes warning and the cloud bursts and it behoves us not to be caught napping. Quartermaster's stores, medical supplies, stretchers, blankets, disappear like ether in an open cup. In their place rifles, equipment, great coats, bayonets and junk of all kinds pour in, until it seems as if it would need the Crystal Palace to hold it all.

Sixth, Adaptability.—Its quarters are as varied as the bits of glass in a kaleidoscope. Perchance the open fields, a tumbledown unsanitary farmhouse, a church, a school house, a granary, a factory, a seminary, rarely—extremely rarely—a chateau. But no matter what the place or what the accommodation, it may be required and often is required to receive patients or wounded within a few minutes of its arrival.

Seventh, Decision.—No matter where it may have opened up, a field ambulance is never safe. Time and time again with accommodation crowded, it may suddenly be subjected to shrapnel or high explosive shells. The question at issue must be decided quickly as the lives of many patients depend upon the action taken. To move or not to move is often the question. Has a suitable place, convenient for carrying your stretcher cases been previously located? Has a shelter been erected where the most serious cases can be conveyed? It is almost a maxim that if the shells once come the recurrence will be more and more frequent. Main roads and cross roads are exceedingly dangerous places, but of course it is not always possible to avoid the use of these, as the choice of suitable buildings is limited and the necessity of good roads for the ambulances is imperative. The enemy have often definite hours for shelling. If they miss look out for trouble, as it will likely come at some unexpected time just when you are full to the limit. Try and evacuate your patients just as quickly as they are dressed. If you are getting overcrowded post an officer—preferably in the road—to commandeer everything possible. Motor lorries, London motor 'buses, motor cars, wheeled transport, nothing comes amiss. It has been our fortune at

least, always to find the drivers only too willing to help you out of your troubles to the fullest extent. An omnibus is ideal for sitting down cases as it accommodates easily and comfortably twenty-five cases, and frequently the day is saved by this timely requisitioning.

The above characteristics are no doubt of academic interest, but the crux of the situation is the practical application in order to obtain the ideal field ambulance. With this in view the following suggestions are made with the ultimate aim of bringing out criticisms and opinions harmonizing or disapproving as the case may be, from other field ambulances, that thus, in the end, much good may be obtained for all. They are based upon our experience with a Canadian field ambulance.

What is required above everything is an operating room staff, separate and permanent, trained to the very highest pitch in personal cleanliness, in proficiency of treatment and bandaging, in handling of instruments and dressings, in knowledge of panniers' contents and in celerity of movement and work; every one knowing what to do, and every man, whether N.C.O. or orderly being duplicated, so that when one half is fatigued the other half can carry on without hitch or hindrance. With the field ambulance as at present constituted this is extremely difficult, if one wishes to give each of the sections an equal share of the work, but by thus making an independent operating staff its members become extremely proficient and in time of stress are invaluable. They are also the means of harmonizing the work of the whole field ambulance, since the tent sub-division of each section in turn work under them, learn the same methods, and thus they can step in to assist at any time without confusion. This also permits of practically all of the sectional equipment being kept closed up, so that the ambulance is ready to move off at a moment's notice if urgently required or if sudden danger arises.

In close association with this are the medical stores, which should be under a man, preferably a corporal, permanently appointed. Here all the reserve dressings, bandages, splints and medicines are kept. A supply for treating two or three thousand should be constantly here, as when parlous times come there is no time or opportunity for drawing more. There were in addition three boxes kept here for advanced dressing stations labelled A.D.S. 1, 2 and 3. They contained dressings, wool, bandages, splints, scissors, soap, collapsible candle lanterns, and iodine. They were of great value, as we had three urgent calls for supplies and were thus able to send them to our A.D.S. without a moment's loss of time, whereas if they had not been previously prepared it might have been very difficult to supply the necessities in time to be of value.

Equally important are trained ambulance orderlies, ten in all, one for each ambulance. It is astonishing the difference between a man who has been acting as an orderly for two or three weeks, and one who is doing it for the first time, even if he is a first-class stretcher-bearer. The preparation of ambulances for stretcher cases, or for sitting, the proper pushing home of the stretcher, the strapping of the stretcher, the disposal of kit, are all little things in which the beginner falls down and loses valuable time. So for this reason I am strongly in favour of permanent men, taken from the ranks of the bearer sub-divisions.

Another equally important part of the work is the returns. Accuracy

combined with rapidity is of supreme importance, as there is no news more anxiously waited for in the home land than the news relating to the welfare of the soldier who has gone through the battle ordeal. Here again precious minutes may be lost over and over again. The following method appeared to work well—one officer was appointed purely to handle admissions and discharges. It was found impossible to admit them in the ordinary way as the wounded came in by fifties and the call from the sentry at operating room door for "one stretcher case" or "two sitting cases" and so on, came far faster than it was possible to admit them, so a good clerk was detailed to the operating room to fill in the "specification tally" from information given by the surgeon dressing the case. A rubber stamp previously bought was used for stamping the tally if serum was injected. When red bordered labels ran out red seal stickers previously bought were used to indicate dangerous cases. The stretcher cases were then taken into one place and the sitting-up cases into another. When the convoy came for evacuation one officer in charge with two assistants, each with Army Book 152, then made duplicate lists of the cases as they were put in the ambulances—a separate page for each ambulance. The duplicate was torn out and handed to the driver with instructions to give it to the officer at the casualty clearing station on arrival. There was thus a triple check, the tally on the patient himself, the original in our possession, and the duplicate given to the driver. The same system was followed in connexion with the sitting-up cases, except when word was received that motor 'buses would be available, then the checkers made lists of twenty-five in duplicate in Army Book 152 and when the 'bus arrived the names were called out, the men paraded and escorted to the 'bus. The duplicate was then handed to the driver. In this way an absolutely accurate record of evacuation and, of course, admissions was kept. These books were collected and handed into the orderly room, one or two at a time, when they were entered into the admission and discharge book. The fact that we handled 5,200 cases in six days speaks for the rapidity with which the work was done, and it was practically impossible to miss anyone who was treated and evacuated through the field ambulance. It also permitted our admission and discharge book being kept beautifully clean and legible, which in itself is invaluable for future records.

Again another branch which should have a permanent staff is the quartermaster's. Every patient that passed through our hands, if his condition permitted, received at least one meal. Somewhere in the neighbourhood of 8,000 extra meals were served during these six days. This was only made possible from the fact that the men in charge were ready for all emergencies and able to handle everything in a rapid and satisfactory manner. This equally applies to the pack store, where confusion would reign supreme unless the men in charge are permanent and thoroughly conversant with their duties.

Another branch requiring a head is, I think, the guard. A permanent provost corporal should be appointed, and, detailed to him, one permanent private from each section. These men become thoroughly proficient in their duties, and are sufficient for day work. An extra picquet is detailed daily for night duty. Hours of duty—two on and four off. In rush times they are specially valuable for the control of incoming and outgoing traffic to prevent congestion.

This has all been an attempt to justify our formation of a so-called headquarters section—its personnel as follows :—

1 .. Officer Commanding
1 .. Quartermaster
1 .. Sanitary Officer } Either of these to be Adjutant; in our case, the Quartermaster
1 .. Transport Officer
1 .. Serjeant-Major (Warrant Officer)
3 .. Quartermaster-Serjeant, Corporal Assistant and 1 private
6 .. Staff-Serjeant, Serjeant, and 4 tent orderlies in charge of operating room
1 .. Pack Store—1 private
1 .. Medical Stores—1 private
2 .. Sanitary Serjeant and 1 private
8 .. Transport Serjeant, 3 grooms and 4 drivers
4 .. Orderly Room Serjeant, 1 clerk and 2 orderlies
10 .. Ambulance orderlies
2 .. Cook, assistant cook
1 .. Provost Corporal
5 .. 1 Lance-Corporal and 4 servants

4 Officers, and 44 N.C.O.s and men.

A, B and C Sections.

Officers	2
Staff-Serjeants	2
Serjeants	2
Corporals	2
Cooks	2
Transport Corporal	1
Police	1
Sanitary	1
Tent	16
Servants	2
Groom	1
Bugler	1
Transport	10
Bearers	24

Each, 2 Officers, and 65 N.C.O.s and men.

A, B and C Sections	201
Headquarters	48
	249

This rearrangement permitted us to have each man in the headquarters section trained to do certain definite duties. In this way, no matter what may arise, I believe, a field ambulance should be able to cope more rapidly with every difficulty, as A, B or C sections or the whole three can be attached at any time without the slighest confusion and with the maximum of increased usefulness. The depletion of the section does not interfere with its capability for work, as it is quite easily able to cope with any detached duty for which it might be ordered.

It will also be noticed that the tent sub-division is relatively larger as compared with the bearer. This is, I take it, very important, as men are only human and the limit for efficient work is soon reached unless they are regularly rested. The tent personnel should be large enough to permit of two shifts, one for day and one for night; better work is done, and rapidity of work greatly increased. With the bearers this is of considerably less importance as their work is practically all done at night, and it is only extremely rarely that they can all be used on account of the difficulty of transportation. In the great majority of cases, two or three stretcher-bearers to each ambulance in addition to the permanent wagon orderly are all that is required.

Lecture.

CHADWICK PUBLIC LECTURE.

PROFESSOR ROGET'S third and last Chadwick Lecture delivered in the Lecture Hall of the Surveyors' Institution on Friday, October 29th, treated of the work mapped out for the Public Health Department of the League of Red Cross Societies in the civil community. The Hon. Sir Arthur Stanley, G.B.E., C.B., M.V.O., Chairman of the Joint Council of the British Red Cross Society and Order of St. John, presided.

The lecturer referred again to the Cannes Conference, held in conjunction with the Convention of Red Cross Societies in Geneva last spring, and also to the Medical Advisory Board of the League which met for the first time in July in the same town.

The work to be undertaken stands divided into seven sections: a section concerned with social diseases, considering more particularly venereal complaints; a section for the prevention of malaria, another for the prevention of tuberculosis, a fourth on preventive medicine, a fifth on child welfare, a sixth on nursing, and the seventh, known as the educational section, comprising propaganda work, publications and statistics.

Considering venereal diseases first, the lecturer pointed out the difficulties attending the inclusion of those affections in Red Cross work, and the greater suitability of the medical officer's intervention along with that of physicians in private or hospital practice. He laid particular stress on the need for safeguarding the dignity of women, perhaps in impressing upon some of them a deeper sense of self-respect than there was at present in many quarters a tendency to observe. While every moral and religious influence should be brought to bear upon the stamping out of the "social evil," he quite accepted the finding of the expert that science is duty-bound to quell that source of human suffering, since it professes itself able to do so with a sufficient allowance of time and the proper enforcement of the necessary regulations.

Passing on to tuberculosis, he described it as the second of the properly so-called "social diseases," for the times were now far distant when phthisis passed for a climatic disease only

He had something to say about the two modes of attacking the disease. The preventive mode of giving to human beings an environment, and a nutrition, as free from germs as possible, should not be applied irrespective of the segregation of tuberculous persons and keeping them apart from the healthy for any necessary length of time.

On the subject of malaria, the lecturer pointed out by what scientific means, the application of which raised no question except that of money and administrative efficiency, it was now possible to restore to salubrity whole tracts of country hitherto a prey to the disease.

Passing on to child welfare and nursing, which, in his opinion, were intimately connected with women welfare, as being particularly the business of

women willing to serve humanity in "terms of their own sex," he showed that the union of the visiting nurse and the mother would afford a proper safeguard of the home, under Red Cross assistance, for no work of social relief could be better suited to the Red Cross organizations in times of peace than child welfare work.

That "preventive medicine" should form the subject of a distinct section in the Public Health Department of the League of Red Cross Societies was not a contention that could raise any dissent. Preventive medicine belonged to every class of social health work and provided, as it were, the armoury whence the scientific means for this crusade could be obtained. There could not be an efficient preventive service without Red Cross laboratories placed at the disposal of the medical practitioner in far greater number than they were at present available.

But perhaps the greatest Red Cross task would be that of education, a task for which literature, lectureships, health libraries, demonstration museums would be required, principally in those unfortunate countries which lagged in the rear of civilziation in all matters connected with hygiene, sanitation and clean housing.

Travel.

FROM MACEDONIA BY OVERLAND ROUTE.

By Colonel S. F. CLARK.
Army Medical Service (Retired pay).

There was decidedly a certain liveliness in the Eastern Mediterranean while the submarine campaign lasted, and one often read in Salonika Force Orders that letters or parcels of such and such a date "had been lost through enemy action." Food and material shared the same fate at times, unannounced, and ships did much intricate navigation among the isles of Greece in order to baffle the U boats. For a long time all travellers to or from Macedonia had to run the gauntlet by sea via Salonika, and were greeted or farewelled there by the cheerless sight of a torpedoed ship beached just outside the boom, but the completion of a new railway line enabled a greatly shortened sea passage to be used. Before this privileged persons had occasionally journeyed by motor car to Santa Quaranta and there taken ship, but this consumed too much petrol for ordinary use.

A note on a trip by the shortened sea route which came into general use for all ranks in 1917, with happenings by the way, may interest some readers.

At noon on April 6, 1918, I left Salonika by rail for England, and next morning arrived at Bralo, a new branch line terminus, where a rest camp for troops in transit was located. The line from Salonika to some extent followed the route taken by the army of Xerxes in his invasion of Greece; it skirted the sea base of Olympus, traversed the beautiful Vale of Tempe, touched

at Larissa, and went through the pass of Thermopylæ. I was the only passenger for home, and was not surprised to find that owing to the heavy fighting in France much uncertainty prevailed at Bralo as to my chances of getting any further. A wire from the base, however, caused me to be added at short notice to a small party which was detailed to go on, so at noon on the 8th we started for the next halting place—Itea. This stage had to be done by road, and we were carried in a convoy of motor lorries which plied between the two camps. The mountain range belonging to Parnassus, whose lofty white peaks almost cast their shadows on Bralo, had to be crossed, and this was made possible by the efforts of British labour companies and of large gangs of local workers who were still employed on the road which they had widened and improved. The drive was through fine scenery, up and up slowly on a zig-zag course until the crest of the ridge was gained, from which the lorries lumbered down on the other side to level ground near Amphissa, where extensive groves of olive trees were traversed. After a four and a half hours' run from Bralo we reached Itea, where we again found much uncertainty as to our next move, as no British ships were expected to arrive.

The camp was near the sea, on the Gulf of Corinth, which looked quite land-locked, and the view that evening lingers in one's memory. To the south was the calm blue water of the gulf, in which a few small islands were picturesquely set, and on its edge were the village of Itea and the hamlet of Kirya. Across the water stood the snow-capped mountains of Morea, silhouetted sharply against the blue sky, with light fleecy clouds floating lazily below their tops. To the east was the plain on which the Pythian games were held, now dark with olive groves or else chequered in squares of green where the young barley was springing, or of brown with black spots, marking the newly turned soil of vineyards dotted by the leafless vines. This area was ended abruptly by rocky hills whose spurs ran down to the sea one behind the other. To the north of these heights and separated from them by a great gorge rose the still loftier crests of the Phocian Alps, dominated by Parnassus, the home of Apollo and the Muses. Here was the main interest of the scene, for high on the southern slopes of the range lay two small villages; one was Chryssos, pictureque but unknown, but the other, perched almost on the edge of the gorge, marked the site of the Oracle of Delphi.

Mythology has it that Apollo founded the Oracle, but his human agents knew the importance of the effect of one's surroundings on the mind, for the place was shrewdly chosen to create a properly receptive atmosphere in all who came to it for inspired information and advice. Pilgrims arriving by water, who stepped ashore at Kirya, and those who journeyed by the passes and valleys of the land, could not fail to be impressed by the physical effort needed to gain their objective, and by the grandeur of the mountains and the blue beauty of the sea. The fame of the Oracle must have been

enhanced not a little by its setting, and also by the belief that it marked the centre of the earth.

Who would have thought that war between England and Germany would bring British officers to Delphi?

Our party consisted of two medical officers of mature years and half a dozen infantry subalterns—young and cheerful—and all eagerly seized the chance of visiting Delphi which was afforded next morning by a lorry going to Chryssos on duty. It took us to that village and back, while the rest of the journey was done on foot. All the way the wealth of flowers was wonderful—they grew everywhere, on the roadside and among the rocks and stones of the hill, in the greatest profusion and variety. There were daisies and dog daisies, poppies of the loudest scarlet, anemones of various colours, white and mauve scabious, pimpernels red and blue, furze, snapdragon and yellow rods, spiderwort and stars of Bethlehem, wild sweet pea, mallows, little yellow asters, and many another that we could not name, pink and blue, yellow and white, beautiful to see, and with their sweetness not altogether wasted.

From Chryssos we began the rough and uphill walk along the stony mountain path to Delphi, two and a half kilometres away, and about half way we sat down in a row to rest and to view the scene. The Baedeker which the camp commandant had kindly lent was produced, and was given to the subaltern on the right of the line to read aloud, but it quickly reached the older men on the left, for the long Greek proper names defeated the youngsters one after the other, and as each man crashed he handed the book to his neighbour hurriedly. The left of the line held firm, however, and concluded a very amusing "turn."

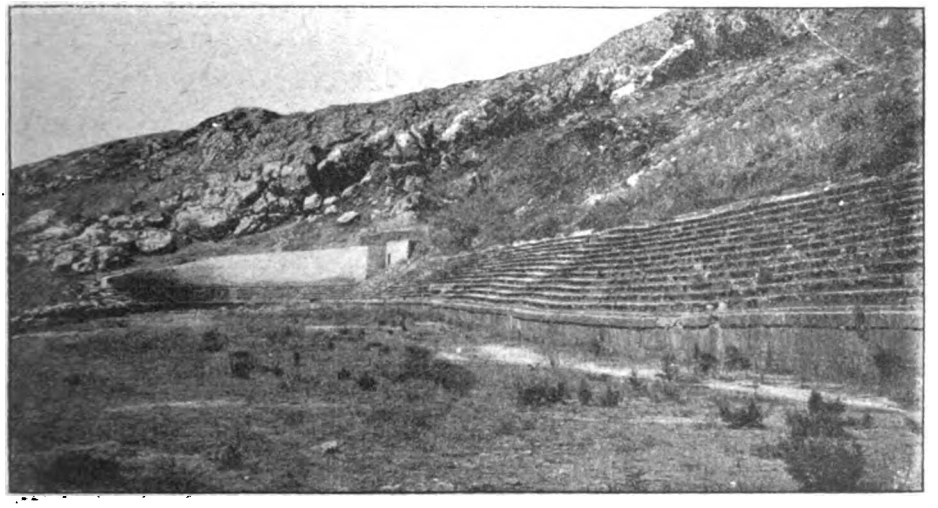
Anon we reached the modern village of Delphi, and walked through it towards the site of its historic predecessor whose ruins have been exposed to view by French excavation. First we visited a museum of local antiquities, and then rounded a corner of the road and found ourselves at ancient Delphi, whose Oracle swayed the acts of men in ages past. The remains were extensive, and the guide who affixed himself to us gave names to everything. We walked up the Sacred Way to the Temple of Apollo, and were greatly interested in the surmised site of the Oracle itself. There was not the least sign of a chasm, but a half underground covered way ran from the temple to the Sibylline Rock, which the guide declared was used by the priestess. It pleased us to believe this and to go through the passage ourselves, which we did without encountering any vapours or feeling any inclination towards frenzy.

Then we entered the wonderfully well-preserved stadium, or sports enclosure, with tiers of stone seats still in place surrounding a grass oval. At one end of the arena long flat grooved stones were sunk flush with the ground, so that the runners' feet might get a firm grip for a good start in the sprints. We used them ourselves in a race that we held in order to

carry on the traditions of the spot. One of the youngsters won it, and the stone seats held no visible spectators.

There was evidence that monopoly in catering is no new thing, for an ancient inscription cut on the wall of the stadium forbade drinks to be brought into the place.

We saw all that was to be seen, including the gorge of the Castalian spring in which the priestess of the Oracle used to bathe before giving a *séance*—and so back to Chryssos and camp, well content with our day among the Shades.



The Stadium at Delphi.

On 10th our party was roused up at midnight for immediate embarkation, and by 2 a.m. on 11th we were on board a French troopship—the "Arcadia"—which sailed at 7 a.m. with no other passengers. We steamed to the west down the Gulf of Corinth, and as we passed Patras a French destroyer joined us, following close in our wake, and after we had gone through the last boom our stern gun was loaded and a seaman stood constantly by it.

We zig-zagged along the coast, passed a group of mine-sweepers at work, met a patrolling seaplane, and after sighting Corfu at dusk steered a course for Italy—the ship and the escort being in complete darkness. At 6 a.m. on 12th Italy was in sight, and three and a half hours later we passed through the boom and entered the fine harbour of Taranto, where the captain told me that his hair had gone grey during the war, and that submarines had been reported at one point on our course, but after we were well past it.

We soon disembarked and separated, for my rank enabled me to travel

on the same evening by the "Rapide" train, while my cheery companions went to the British rest camp which was established at Taranto, to await a troop train—the usual way in which personnel travelled through Italy and France.

The rest of the journey was done by the ordinary railway, mainly by night, and through the Mont Cenis tunnel—giving a day in Rome and Turin and four hours in Paris. Havre was reached at 10.30 p.m. on 15th, too late to catch the boat, so I slept at a hotel and did not wake till noon next day. On the evening of 16th I sailed on the London and South Western Railway steamer, reached Southampton at 7 a.m. next morning, and reported at the War Office by midday, just eleven days from Salonika—exactly the time taken to go out by the all sea route, but a much safer trip.

Current Literature.

Bacteriology.—In the *Indian Journal of Medical Research*, vol. vii, No. 3, January, 1920, Dorothy Norris describes the preparation of a culture medium from caseinogen. It is cheaper, easier and quicker to prepare than a meat medium, and the yield of bacteria (typhoid, paratyphoid, cholera) is equally good.

Influenza.—"Bacteriological Investigation of Influenza," by H. R. Malone, *Indian Journal of Medical Research*, vol. vii, No. 3, January, 1920. The blood serum of influenza patients possesses the power of agglutinating Pfeiffer's bacillus (homologous strain) in eighty-two per cent of cases. Heterologous strains are agglutinated in forty per cent of cases. The serum of healthy persons does not agglutinate Pfeiffer's bacillus. Agglutinins appear during the first week of illness and persist for at least five weeks.

In another paper by the same author it is shown that ninety-two per cent of the strains of Pfeiffer's bacillus, when grown on suitable media, produce indol, a property not possessed by other hæmophilic organisms present in the respiratory tract, in health, or in influenza. The indol reaction can be used for identifying Pfeiffer's bacillus in pure cultures. The method described promises to be of considerable assistance in the not easy task of recognizing Pfeiffer's bacillus in the secretions of the respiratory tract of influenza patients.

Tuberculosis.—"Infection et Vaccination par Voie trachéale," by A. Besredka, *Annales de l'Institut Pasteur*, vol. xxxiv, No. 6, June, 1920. The pulmonary apparatus is powerless to hinder toxins and soluble poisons from penetrating rapidly into the general circulation, but it offers a strong barrier to the invasion of viruses having a definite form. By comparing the resistance of an animal to inoculation of a virus by the tracheal and venous routes respectively, one can gauge the importance of the pulmonary barrier. This natural pulmonary resistance to invasion can be reinforced by the direct application of vaccines to the respiratory tract, i.e., one can create an artificial local immunity.

Massive and repeated doses of tubercle bacilli are tolerated by the respiratory tract. Can this natural local immunity be increased by repeated intratracheal injections? It is not possible to give any definite answer at present, but it can be asserted that the injection of tubercle bacilli by the tracheal route gives rise

to the production of more abundant and more persistent antibodies than can be obtained by any other method of inoculation.

Cholera.—*Ibid.*, "De la Pathogénie du Choléra" (3me mémoire), by G. Sanarelli. The toxin of cholera vibrios is represented by the proteid of the vibrios themselves. This proteid can be liberated by shaking solid cultures of cholera, grown in a freely alkaline medium (killed with toluene) with a weak solution of "pancréatine." This only dissolves the covering membrane of the vibrios, leaving the contents intact, with their antigenic and toxic properties: these contents remain in a colloidal state in the liquid.

The proteid of the cholera vibrio only exhibits *immediate* toxic power when introduced into the blood-stream (of guinea-pigs). In this case the minimum lethal dose is equivalent to that of living cultures: its toxic action is not exerted directly on the nervous centres, as some writers have stated, but it attacks the alimentary canal, producing an acute fatal gastro-enteritis.

These intestinal lesions resulting from the intravenous injection of cholera proteid are exactly similar to those resulting from the intraperitoneal injection of a fatal dose of vibrios killed by heat. This fact makes one doubt whether death of guinea-pigs following the intraperitoneal injections of living vibrios is caused by an inflammatory process of the peritoneum, as is generally believed.

In rabbits the toxic action of the proteid, even if injected into the peritoneum, has a selective action on the alimentary canal giving rise to a gastro-enteritis—acute, subacute, or chronic—according to the dose administered. These inflammatory processes are always accompanied by an enormous multiplication of intestinal *B. coli*, and a general bacillary infection may ensue.

The toxic action produced by the proteid of cholera vibrios on laboratory animals, except for the severe lesions in the alimentary canal, does not give rise to a condition in any way resembling the "algid state" of cholera. There is a doubt, therefore, whether one is justified in regarding the proteid extracted from cholera vibrios as the real "cholera poison."

Correspondence.

DESTRUCTION OF MOSQUITO LARVÆ BY FISH.

TO THE EDITOR OF THE "JOURNAL OF THE ROYAL ARMY MEDICAL CORPS."

SIR,—I have read with great interest Major Boyd's article in the November Journal, on the destruction of mosquito larvæ by fish. His conclusions are supported by observations obtained from quite another point of view, namely, the sporting one.

All fishermen, and particularly those who are "dry fly" enthusiasts, are aware of the fact that if you watch the large trout in a clear chalk stream when a hatch of Ephemeridæ is going on, the fish can be seen to rise and seize these flies as they flutter past on the surface. Insects of the Ephemeridæ class form a large part of the food of trout in these conditions. In their first winged state they are known to fishermen as "duns," and the artificial floating flies tied to imitate them are called "olive dun," "little iron blue dun," etc., according to the variety which they imitate.

If trout thus feeding on "duns" are closely watched, it will be seen, however, that they move from side to side, picking up and feeding on something which is

not on the surface, but being carried past underneath. The fish even neglect the floating duns drifting right over their heads in order to pick up this something under water. This something is the larval stage of the Ephemera, known to fishermen as a "nymph," and it exactly corresponds to the larval stage of the mosquito when it is coiled up motionless under the surface just before its metamorphosis into the winged stage. In the same way the Ephemeræ larvæ on which the trout are feeding have arrived at the stage when they are just about to split up the back of their larval skin and emerge as a winged fly.

The only difference, so far as I am aware, in the life-history of the Ephemeridæ and the closely allied gnats to which the mosquitoes belong, is that in the case of the Ephemera the winged fly or "dun" which emerges from the larva is not the final or perfect form of the insect, but is known as the sub-imago. The last or perfect stage imago is an insect with bright transparent wings, like the dragon-fly. They are to be seen in swarms rising and falling in the air, over the pools and shallows of a trout stream on summer evenings, where the females deposit their eggs and having thus finished their cycle of life they die. These forms are known to fishermen as the "spinners."

To return however to the larval form. It has been proved that trout do feed on them very largely. Various expert angler naturalists having watched them as described above, neglecting duns floating over them on the surface to pick up small objects being carried past in the current, have caught these trout and identified the Ephemeræ larvæ as constituting the principal contents of the stomach. The late F. M. Halford, one of the best known writers on angling subjects, describes such examinations in the "Dry Fly Man's Handbook" and "Modern Development of the Dry Fly." Skues in his book, "Minor Tactics of the Chalk Stream," does the same.

I have also found larvæ in the stomachs of trout myself. In fact the latest development of dry fly fishing, as introduced by Skues in the latter book, is to have artificial flies made closely to imitate the various larvæ of the Ephemeridæ and to fish them "wet," that is to float them over the nose of a feeding fish, not on the surface but under water.

It therefore seems to me that if, as has been proved, you can watch trout devour ephemeridal larvæ by hundreds, and then prove that they were ephemeridal larvæ and nothing else by finding them in the trout's stomach after you have caught him, there is at least a very high degree of probability that fish under natural conditions will display an equal degree of avidity in devouring the larvæ of the closely allied species, the gnats and mosquitoes.

I am, etc.,

J. B. WILSON,
Major-General.

Headquarters, York, November 13, 1920.

ERRATUM.

December number, Correspondence, page 503, line 10, for *brigade* read *big*.

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Journal
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Original Communications.

NOTE ON THE INFLUENCE OF DIET ON THE ENERGY EXPENDITURE IN WORK.

BY J. B. ORR, D.S.O., M.C.
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AND

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INTRODUCTION.

IN 1918, Cathcart and Orr (1919) (1) conducted an investigation to determine the energy expenditure of the infantry recruit in training. Some observations which were made in the course of the investigation seemed to indicate that the amount of energy expended per unit of work is influenced by the nature of the preceding meal. It was impossible during the course of the inquiry, owing to its urgency, to devote more time to this question, but the few results obtained seemed to warrant further investigation, and the experiments recorded here were therefore carried out.

NATURE AND METHODS OF INVESTIGATION.

Following the taking of food there is a stimulation of metabolism which is shown by an increased heat production in the body. Thus in a subject at rest after a very high protein meal the heat output may be almost fifty per cent higher than in the preceding post-absorptive state, i.e., when food is not being absorbed from the intestine. The increase is somewhat less after a high carbohydrate meal and least after a high fat meal. When work is done there is of course an extra heat production due to the work.

In work after a meal therefore there is in addition to the basal metabolism, i.e., the rate of metabolism at rest in the post-absorptive state, an increased metabolism due to food and a further increase due to work.

The object of the investigation was to determine (1) whether there is a simple summation of extra metabolism due to food and extra metabolism due to work, or (2) whether the energy evoked due to food is available for work production, or (3) whether the increased rate of metabolism due to food involves also an increased rate in the additional metabolism due to work.

As the energy yielding constituents of food affect the rate of metabolism to different degrees and possibly by different means, it was necessary to determine the energy expenditure on a constant amount of work in different experiments in which either protein, fat or carbohydrate predominated in the preceding meal. To obtain a common basis of comparison the resting metabolism and the energy expenditure on the given amount of work were determined in the post-absorptive state immediately before the meal in each case. The procedure was as follows: In the morning about fifteen hours after the last meal, the subject being in the post-absorptive state, the resting metabolism—ten-minute periods—and immediately thereafter the energy expenditure—four-minute periods—on the fixed rate of work were determined. The meal was then taken, and after an interval of ninety minutes the resting metabolism and the energy expenditure on the work were again determined.

The work consisted of marching along a corridor at the rate of 100 yards per minute. In covering the measured distance a uniform rate of stepping of 120 per minute was maintained. The subject was allowed to march for a preliminary period of ten minutes to ensure that a uniform rate of progression had been reached before the sample of expired air was drawn.

The energy expenditure was estimated by the indirect method of calorimetry. The expired air was collected in a Douglas bag, and the analysis done with Haldane's apparatus. The oxygen figures and the Zuntz values were employed in calculating the results. The complete apparatus and method of calculation were as described by Cathcart (1918).

The test meals had each 50 grammes of oatmeal, to which was added for the high protein meal 100 grammes "plasmon" (about eighty per cent casein), for the high carbohydrate 80 grammes of cane sugar, and for the high fat 35 grammes margarine. The protein and carbohydrate meals had each about 540 calories, the fat about 480. Preliminary trials had shown that the subject would not eat more than thirty-five grammes of margarine at once without complaining of nausea.

Experimental Data.

The only figures discussed are those showing the energy expenditure on the work. To reduce the size of the table, only the number of calories

and the respiratory quotients are given. From these the O_2 and CO_2 figures can be calculated. Each result for lying is the average taken with an interval of a few minutes.

SUBJECT: T. B., AGED 26; WEIGHT, FIFTY-SEVEN KILOGRAMMES; HEIGHT, 5 FEET 4·5 INCHES.

Date	Lying		Marching		Increase due to work	Diet
	Respiratory quotients	Calories per minute	Respiratory quotients	Calories per minute	Calories per minute	
—	0·885	1·11	0·89	4·91	3·80	Post absorptive
			0·87	4·78	3·67	,,
—	0·975	1.26	0·94	4·82	3·56	Carbohydrate
			0·95	5·00	3·74	,,
—	0·79	1·17	0·86	4·85	3·68	Post absorptive
			0·78	5·16	3·99	,,
—	0·75	1·43	0·83	5·43	4·00	Protein
			0·80	5·28	3·85	,,
—			0·90	4·80	3·69	Post absorptive
	0·85	1·11	0·93	4·73	3·62	,,
—	0·87	1·18	0·79	5·05	3·87	Fat
			0·81	5·18	4·00	,,
			0·80	5·09	3·91	,,
—	0·845	1·17	0·93	4·58	3·41	Post absorptive
			0·84	5·03	3·86	,,
—	0·93	1·29	0·85	5·09	3·81	Carbohydrate
			0·89	5·10	3·82	,,
			0·86	5·18	3·90	,,
—	0·86	1·21	0·86	4·98	3·77	Post absorptive
			0·87	5·13	3·92	,,
—	0·86	1·24	0·88	5·13	3·89	Protein
			0·89	5·12	3·88	,,
			0·88	5·04	3·80	,,
—	0·83	1·03	0·90	4·87	3·84	Post absorptive
			0·87	4·98	3·95	,,
—			0·86	5·46	4·18	Protein
	0·78	1·28	0·85	5·41	4·13	,,
—	0·85	1·07	0 88	4·79	3·72	Post absorptive
			0·88	5·04	3·97	,,
—	0·825	1·22	0·87	4·58	3·36	Fat
			0·83	5·21	3·99	,,
			0·81	5·01	3·79	,,
—	0·80	1·06	0·89	4·91	3·85	Post absorptive
			0·86	4·80	3·74	,,
—	0·83	1·18	0·88	4·76	3·58	Fat
			0·85	4·90	3·72	,,
			0·84	4·89	3·71	,,
—	0·86	1·02	0·91	4·93	3·91	Post absorptive
			0·94	4·68	3·66	,,
—	0·94	1·32	0·92	5·00	3·68	Carbohydrate
			0·93	4·92	2·60	,,
				4·68	3·36	,,

The following table gives the averages of the results obtained in the post-absorptive state and after the meals :—

AVERAGES IN CALORIES PER MINUTE.

	Post absorptive			After meal		
	Lying	Marching		Lying	Marching	
		Gross	Net		Gross	Net
Carbohydrate ..	1·11	4·82	3·71	1·29	4·94	3·65
Protein	1·14	4·99	3·86	1·32	5·27	3·96
Fat	1·08	4·85	3·77	1·19	4·96	3·77

Discussion of Results.

The individual results show considerable variation under what are as nearly as possible identical conditions. It is impossible to march in an absolutely straight line or to lift the foot the same height at every step. Even in lying differences in the degree of tension of the muscles and involuntary movements give rise to variations in the energy expenditure. In view of these variations the average results of such a comparatively small number of experiments must be regarded with caution. Certain points are however brought out sufficiently clearly to warrant discussion.

The average gross heat production in marching in the post-absorptive state is 4·89 calories per minute. After meals the average is 5·06 calories. After the protein meal the gross energy expenditure is 5·27 calories per minute as against 4·94 and 4·96 for carbohydrate and fat respectively. An increase in the gross heat production following the ingestion of protein is noted by Cathcart and Orr (1919) (3).

The *net* energy expenditure due to work following the different meals is shown by the following table :—

Table showing Net Expenditure on Work in Calories per Minute.

Meal	Increase due to work. In post-absoptive state	After meal	Differences
Protein..	3·86 ..	3·96 ..	+ 0·10
Carbohydrate	3·71 ..	3·65 ..	− 0·06
Fat	3·77 ..	3·77 ..	—

Protein.—After the high protein meal the increase due to the work is 3·96 calories, as compared with 3·86 in the preceding post-absorptive state. There is thus more than a summation of extra metabolism due to food and that due to work. There has been an increased rate in the additional metabolism due to work causing a greater heat production per unit of work.

Carbohydrate.—The increase due to work is here 3·65 calories per minute, as compared with 3·71 in the preceding post-absorptive state. The heat output per unit of work is thus 0·06 calories per minute less after the meal. Either the muscles work more economically with carbohydrate as fuel or part of the increased metabolism due to food is available for work production.

Fat.—After the high fat meal there seems to be a simple summation of extra metabolism due to food and that due to work.

Rubner (1910) investigated the influence of diet on work. On a diet of 600 grammes cane sugar the increase due to work (100,000 kilogram-metres) was 845 calories. On a high protein diet the increase was 855 calories. This is a smaller difference than that obtained by us. The small difference obtained by Rubner is probably due to the fact that he dealt with the twenty-four-hour periods. After the ingestion of carbohydrate the increase in metabolism is of comparatively short duration from three to seven hours, varying with the amount given and the previous diet: Magnus-Levy (1894), Gephart and Du Bois (1915) and others. The increase following protein ingestion on the other hand is much more prolonged. Cathcart and Orr (1919) (3) found that the

stimulus due to ingestion of protein was continued into the post-absorptive state, i.e., over fifteen hours after food. The post-absorptive heat output after a high protein diet was 44·8 calories per square metre as against 35·6 after carbohydrate and 40·9 after a mixed diet. This observation has been confirmed by Krogh and Lindhard (1920). In a twenty-four-hour period therefore the work is superimposed not upon the highest point of the rise due to carbohydrate, but on an average rise of twenty-four hours, which would include a period of low metabolism; whereas in the case of the protein the rise due to food being more prolonged, the work would be superimposed upon an average that would approximate more nearly to the maximum rise. That this explanation seems valid is shown by the fact that the increase in resting metabolism found by Rubner due to the ingestion of 600 grammes cane sugar is only 2·4 per cent, whereas the average increase found in these experiments, in which the determination was made for a short period on the second hour after eating, is 20·6 per cent. As the net expenditure of energy, i.e., the amount expended on the work alone, is the gross expenditure minus the resting expenditure, the low output at rest found by Rubner after the ingestion of the carbohydrate gives a high figure for the increase due to work on carbohydrate diet, and makes it approximate to that found on the protein diet.

Benedict and Murschhauser (1915) found that "the heat production per unit of work is practically independent of the taking of food." They note, however, an increase in the heat production per unit of work with the protein diet as compared with the carbohydrate diet, amounting to approximately nine per cent on the low speed (about 70 metres per minute) and to three per cent on the high speed (110 to 140 metres per minute). The percentage increase obtained in our experiments is approximately 8·5 per cent at 100 yards per minute.

A very marked reduction in the heat output per unit of work after carbohydrate as compared with the preceding post-absorptive state has been shown by Anderson and Lusk (1917). In a dog after taking 70 to 100 grammes of glucose the increase due to work was 0·550 kilogram-metres per kilo body weight per metre travelled as against 0·580 in the previous post-absorptive state and 0·587 following the ingestion of meal.

Since these experiments were completed, Krogh and Lindhard (loc. cit.) have shown by a series of excellently conducted experiments that in the post-absorptive state the output of heat per unit of work is markedly less following a heavy carbohydrate diet than following a fat diet. They conclude that work is more economically performed on carbohydrate than on fat, and suggest as a reason that fat may be changed by an exothermic process to some body allied to carbohydrate before being catabolized. Whether the reason given for the difference be correct these results certainly show that for work production fats and carbohydrates are not isodynamic.

In the present experiments where the work was superimposed about the highest point of metabolism following food ingestion, the reason for

the different result following the different meals may partly be due to the different nature of the stimulus produced by the food.

The specific dynamic action of protein has been shown by Lusk (1913) to be due to a direct chemical stimulus produced by certain amino-acids. This stimulus seems to persist during work, causing an increased rate on the additional metabolism due to work. In the case of carbohydrate and fat the stimulus following ingestion of food appears to be due to a plethora of metabolizable material, Lusk (1917). The increased consumption of material during work would reduce the relative excess and as the muscles tend to metabolize the carbohydrates first (Lusk, loc. cit.), the increase due to this constituent would tend to disappear earlier than that due to fat, so that the gross output on work following a high carbohydrate meal and consequently the net output would tend to be less than following a fat meal.

It should be noted that these conclusions are drawn from data obtained from work in the second and third hour after food, and further that the work is of short duration, not more than half an hour including the preliminary period. They are therefore not comparable with results obtained at a different period relative to ingestion of food, or after a long period of work during which the plethora of metabolizable material causing the rise in metabolism after food would tend to have disappeared.

Summary.

(1) The expenditure of energy per unit of work performed is influenced by the nature of the preceding meal.

(*a*) Following a high protein meal the increase due to work is *greater* than in the preceding post-absorptive state.

(*b*) Following a high carbohydrate meal the increase due to work is *less* than in the preceding post-absorptive state.

(*c*) Following a high fat meal there appears to be a summation of extra energy expenditure due to food and that due to work.

(2) It is suggested that the difference in the results obtained in these three cases is due to a difference in the mechanisms of stimulation involved in the increase of metabolism following the ingestion of protein and of carbohydrate and fat.

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THE PARATYPHOID "C" BACILLUS AS A CAUSE OF PARATYPHOID FEVER.[1]

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Bacteriological Investigations in Macedonia, 1916-17-18.

In 1916, Professor Ludwig Hirschfeld, bacteriologist-in-chief to the Royal Serbian Army, isolated by blood culture a bacillus which, for reasons about to be defined, he labelled "Paratyphoid C." The patients from whom the organism was cultivated were suffering from "enterica," but no known bacillus of the enterica group was isolated and no serological confirmation was obtained. Professor Hirschfeld considered that the organism was distinct from the known paratyphoid bacilli isolated from the Serbian soldiers suffering from enterica, and he decided to add this bacillus to his preventive vaccine. In December, 1916, a vaccine was prepared in his laboratory at Sedes which contained *B. typhosus* and paratyphoid bacilli A, B and C, and *V. choleræ*. This vaccine was employed in the Serbian army for preventive inoculation in 1916, 1917, and 1918. In December, 1916, a bacillus was obtained by blood culture from a Serbian soldier at an Anglo-Serbian hospital suffering from enterica, and as it was found to be atypical it was sent to one of us (L. S. D.) for further investigation. This organism proved to be a strain of the para C. bacillus. An antiserum which was prepared with this strain of para C. corresponded to the para C. antiserum supplied to us by Professor Hirschfeld, and the organisms were in all respects similar.

It was decided to prepare a para C antigen for the laboratories in Macedonia similar to those employed for the typhoid and paratyphoid A and B reactions at the Central Laboratory, and also a supply of para C antiserum. At subsequent periods this organism was isolated by blood culture from Serbian soldiers (six) in Anglo-Serbian hospitals, and further strains were obtained from the fæces of Serbs and others (ten) who were suffering from severe diarrhœa or enterica. The organism was not isolated by us or our co-workers from the urinary tract. It is now known that, in addition to typical enterica, the *B. paratyphosus* C may give rise to

[1] Reprinted from the *Lancet*.

infective conditions, such as severe diarrhœa, broncho-pneumonia, and general sepsis.

Castellani,[1] in an article on typhoid infections in the "Adriatic-Balkan Area," refers to a number of "atypical or mixed enterica infections." He states that six strains were isolated with the cultural characteristics of the *B. paratyphosus* B, but serologically distinct, and three strains culturally similar to the paratyphosus A, although distinct serologically.

Archibald, Hadfield, Logan, and Campbell,[2] in their report on the diseases affecting the troops in the Dardanelles, state that out of 147 cases of enterica, 21 were due to *B. typhosus*, 41 to *B. paratyphosus* B, and 70 to *B. paratyphosus* A, while 15 inagglutinable para A strains and 14 para B were also obtained.

Kennedy,[3] in an article in the JOURNAL OF THE ROYAL ARMY MEDICAL CORPS, reports that in 1914 at the Enteric Convalescent Depôt at Naini Tal he found five inagglutinable strains by blood culture, resembling *B. paratyphosus* A or B.

Macadam,[5] Mackie and Bowen[4] isolated a bacillus in Mesopotamia which appears to be identical with the *B. paratyphosus* C of Hirschfeld. Macadam[5] isolated this bacillus from seven cases by blood culture, and on two occasions post mortem (one from lung and one from bile).

Mackie and Bowen[4] isolated the para C bacillus from 12 cases, 10 from the blood stream, 1 from the urine, and 1 from the liver. The authors state that the paratyphoid C bacillus does agglutinate with some samples of antiparatyphoid B serum to low titre, and also that the para B co-agglutinins are removed from the para C antiserum by the para C bacillus. Macadam noted on several occasions zones of inhibition of agglutination with the para C reaction. Neukirch,[6] while working with the German army refers to his findings in Turkey. He cultivated from the blood, urine, and fæces, bacilli allied to the paratyphoid B bacillus, but

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[1] Castellani: Typhoid and Allied Infections in the Adriatic-Balkan Area, *Ann. Med. Nav. and Colon.*, 1916, November-December, vol. ii, pp. 453-461.

[2] Archibald, R. G., Hadfield, G., Logan, W., and Campbell, W.: Reports on the M. and H. Laboratories, dealing with the diseases affecting the troops in the Dardanelles, JOURNAL OF THE ROYAL ARMY MEDICAL CORPS, June, 1916, vol. xxvi, pp. 695-724.

[3] Kennedy, J. A., Lieutenant-Colonel Royal Army Medical Corps: Inagglutinable Paratyphoid Bacilli (Paratyphoid C) in India, JOURNAL OF THE ROYAL ARMY MEDICAL CORPS, August, 1918, vol. xxxiii, p. 190.

[4] Mackie, F. P., Major, Indian Medical Service, and Bowen, G. T., Captain, Royal Army Medical Corps: Note on the Characters of an Anomalous Member of the Paratyphoid Group met with in Mesopotamia, JOURNAL OF THE ROYAL ARMY MEDICAL CORPS, August, 1919.

[5] Macadam, W: An Account of an Infection in Mesopotamia due to a Bacillus of the Gaertner Paratyphoid Group, JOURNAL OF THE ROYAL ARMY MEDICAL CORPS, August, 1919.

[6] Neukirch, Paul: Ueber menschliche Erkrankungen durch Bazillen der Glasser-Voldagsengruppe in der Turkie, *Zeitsch. für Hygiene und Infektions*, 1918.

serologically distinct. Although he does not give the name para C to these organisms, it is probable from his results that some of his strains were identical with the bacillus of Hirschfeld. On clinical evidence some of the cases were typical enterica, others were dysenteric in character. Dienes and Wagner[7] also obtained similar findings to those recorded by Neukirch.

Garrow[8] has published a case recently of a paratyphoid C infection which occurred in East Africa. The patient presented the clinical features of a typical enterica infection. The paratyphoid C bacillus was recovered from the blood-stream and the patient's serum contained specific agglutinins for this organism. No paratyphoid B agglutinins were present.

Fatal Cases.

We were able to obtain details of two cases of fatal paratyphoid C infection in the Balkans, although other cases no doubt occurred.

Case 1.—Macedonian labourer. Investigated by Captain J. Anderson, R.A.M.C. *B. paratyphosus* C was isolated by blood culture from this patient who was profoundly ill with "enterica," and subsequently died. At the autopsy the spleen was found to be much enlarged, very soft, and congested. There was no intestinal ulceration, but marked patchy congestion of the intestinal wall.

Case 2.—A Macedonian woman was admitted to hospital at Vodena, and died on the eighteenth day after a severe illness. This patient was diagnosed clinically as enterica. No malarial parasites were found in the blood film, and the cerebrospinal fluid was normal in all respects. An agglutination reaction on the thirteenth day of the disease gave a 50/5000 reaction to paratyphoid C, while two days later it reached 125/5000, but no reaction occurred with the typhoid, para A, or para B antigens. No further observations were possible, as the patient was many miles away from a British unit.

Agglutination Reactions obtained in Macedonia.

Captain Anderson, bacteriologist to an Anglo-Serbian Hospital, made the following observations:—

He examined the blood of 104 patients for evidence of typhoid and paratyphoid A, B, and C agglutinins with the antigens supplied by us. Of these patients, 11 were British, 9 French, 58 Serbians, and the remainder included the "mixed bag" of people met with in the Balkans.

Only two out of a total of fifty-eight Serbians gave a reaction to the para C antigen. In the first case the Serb had been inoculated against

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[7] Dienes, L., und Wagner, Richard: Uber Paratyphus B-infektionen, *Zeitsch. für Hygiene und Infektionskr.*, 1918.

[8] Garrow, R. P.: A Case of Paratyphoid "C" Fever in East Africa. The *Lancet*, June 5, 1920.

the enterica group one month previously with Hirschfeld's mixed vaccine and gave a reaction of 50/5000 for para C, 50/15000 for typhoid, and 50/10000 for para A, but no para B reaction. In the second case the Serbian soldier had been inoculated against the enterica group one year previously, and showed a 25/5000 reaction to para C, a slightly greater typhoid and paratyphoid B reaction, but none to para A. Further, although eight cases gave a reaction of 1 in 100 or over with our typhoid antigen, and one case to 1500/8000 with the para B there was no reaction at the lowest limit with the para C antigen.[9]

To elucidate further the question of degree of response to the para C portion of the quadruple vaccine this organism was embodied in the vaccine to be employed for the inoculation of twenty volunteers amongst the Bulgar prisoners, while the remainder received the triple vaccine. The blood of each man was tested for his agglutination response to typhoid, and para A, B and C before inoculation, and again ten days later. The local and general effects of the quadruple vaccine were considerable in many cases, while in all a definite local reaction occurred. In five cases pyrexia exceeded 100° F. on the second day after the inoculation, but in two of these men it was probably malarial in origin. In every instance enlargement and tenderness of the axillary glands occurred.

TABLE I.—Agglutination Response to One Dose of Quadruple Vaccine in Bulgarian Soldiers.

Case	Agglutinin response before inoculation				Agglutinin response 10 days after inoculation			
	T.	A	B	C	T.	A	B	C
1	50	0	0	0	200	100	0	0
2	50	200	0	50	50	300	0	100
3	0	0	0	0	100	100	50	0
4	100	0	0	0	100	100	50	0
5	50	50	0	0	50	100	50	0
6	0	0	0	0	50	50	0	0
7	0	0	0	0	200	50	50	0
8	0	0	0	0	—	—	—	—
9	50	0	0	0	50	100	0	0
10	0	0	0	0	0	50	100	0
11	50	0	0	0	100	100	0	0
12	50	0	0	0	200	100	0	0
13	0	0	0	0	100	100	50	0
14	0	0	0	0	100	100	200	0
15	0	0	0	0	100	50	1,000	0
16	50	0	0	0	200	50	100	0
17	0	0	0	0	50	50	50	0
18	50	0	0	0	50	50	200	0
19	50	0	0	0	50	50	50	0
20	50	50	0	0	200	200	1,000	0

End-point of antigens, typhoid, 15,000; A, 10,000; B, 8,000; C, 5,000.
Note.—0 = 1/25, no reaction.

[9] It is a matter of considerable difficulty to obtain reliable information concerning preventive inoculation among the Serbian soldiers.

Agglutination Response.

It will be seen from Table I that of the 20 Bulgars whose blood was tested before inoculation 10 gave a 50/15000 reaction to the typhoid antigen, and 1 a 100/15000, while only 3 reacted to the para A antigen, one of them to the extent of 200/10000. No reaction occurred with the para B antigen, and in only one instance with the paratyphoid C. The agglutination response, therefore, to the paratyphoid antigens was feeble or entirely absent. No evidence was obtainable as to whether these men had been inoculated previously with a triple vaccine, although they had received a typhoid vaccine some months previously.

The inoculation of our quadruple vaccine excited an active response to the T, A and B antigens, but a C reaction occurred in only one instance (Case 2); here a reaction of 50/5000 was obtained before inoculation, which rose to 100/5000 ten days after the injection of the vaccine. In two instances a B reaction of 1000/8000 was produced, but no C reaction was obtained.

The same strain of para C bacillus was employed for the preparation of the vaccine and antigen.

These agglutination reactions with the Bulgar prisoners agreed with our findings obtained with the Serbian soldiers, and may serve as an explanation for the absence of a reaction in the latter, although we had believed them to be inoculated with Hirschfield's mixed vaccine. It must be remembered, however, that it was possible to test the agglutination reactions among the Bulgars on one occasion only after the injection of the vaccine, as they were required for military purposes. Further, the highest agglutination reaction observed among the cases of para C infection by us was 500/5000.

Animal Inoculations.

A rabbit was inoculated subcutaneously with 50 million of each organism in a quadruple vaccine, nine days later with 100 million, and again eight days later the dose was repeated. The agglutinin response is tabulated in Table II.

TABLE II.—Rabbit inoculated subcutaneously with T, A, B, C Vaccine.

T.	A	B	C		
0	0	0	0	..	Before inoculation.
		50 *Million T. A, B, C Subcutaneously.*			
100/15000	100/10000	50/8000	200/5000	..	9 days after first inoculation.
		100 *Million T. A, B, C Subcutaneously.*			
800/15000	400/10000	400/8000	1200/5000	..	8 days after second inoculation.
800/15000	600/10000	600/8000	1500/5000	..	9 days after third inoculation.

A second rabbit was inoculated subcutaneously with 10 million of each organism employed in the quadruple vaccine, and seven days later with 20 million, but a similar agglutination response was obtained as shown in Table II.

The two rabbit experiments just referred to show that these animals give a response to each member of the quadruple vaccine when the immunization has been obtained with large or average doses.

TABLE III.—To show the Agglutinin Content of Immune Rabbit Sera titrated with our Standard Antigens as used in the above Experiments.

Serum	Antigen	Agglutination end-point	Serum	Antigen	Agglutination end-point
Para C	Para C	5000/5000	Para A	Para B	100/10000
Para C	Para B	100/5000	Para A	Para C	0/10000
Para B	Para B	8000/8000	Typhoid	Typhoid	15000/15000
Para B	Para C	250/8000	Typhoid	Para C	0/15000
Para A	Para A	10000/10000	Typhoid	Para B	0/15000

Cultural Tests.

Every strain of para C tested by us has shown the same cultural reactions, and, further, these reactions have remained constant in stored laboratory cultures.

The organism is a motile Gram-negative bacillus. It ferments glucose, mannite, maltose, dulcitol, and sorbite with gas production, while cane sugar and lactose remain unchanged. Litmus milk is first acidified, the medium gradually returns to neutral point, and finally is rendered alkaline in three to four days. No strain which we have investigated has produced indol.

Since the above observations were made in Macedonia we have further investigated the serological reactions of the para C bacillus and compared its antigenic properties with the other members of the enterica group of organisms. Rabbit antisera have been prepared and the reactions to the enterica group, including the para C bacillus, have been studied. Three types of vaccines were employed: (1) heat-killed; (2) formol-killed, and (3) vaccines grown in 1 per cent dextrose[10] and killed with formalin. Para C vaccines have also been employed for the inoculation of men who offered their services, and the antigenic properties were observed in these healthy individuals, many of whom were ex-soldiers and whose sera contained typhoid and paratyphoid (A and B) agglutinins.

Methods of Preparation of Vaccines.

The vaccines employed by us in these investigations were made as follows:—

(1) *Heat-killed Vaccines.*—A twenty-four hour agar culture of this organism was emulsified in normal saline, filtered through fine linen, and heated to 56° C. for one hour. The vaccine was then placed in the ice

[10] This vaccine will be called subsequently in this paper the "acid dextrose vaccine."

chest, and later tested for sterility. Suitable dilutions of the emulsion were made with saline containing 0·25 per cent carbolic acid.

(2) *Formalin-killed Vaccines.*—A twenty-four hour agar culture was emulsified in normal saline and filtered as above. To the emulsion 0·1 to 0·14 per cent of formalin was added and the emulsion placed in the ice safe till sterile. Suitable dilutions were made as above.

(3) *Acid Dextrose Vaccines.*—Organisms were grown in one per cent dextrose in peptone water and the tubes were incubated for twenty-four hours. The acidified medium was centrifugalized and the supernatant fluid discarded. The deposit of organisms was diluted with saline containing 0·1 to 0·14 per cent of formalin and treated subsequently as in method 1.

Some of the volunteers received one type of vaccine only, and others one type followed by another. Rabbits were also inoculated with the vaccines and the agglutinin response tested.

The antigens used were made as follows :—

The organism was subcultured daily for ten days to obtain an active growth. Agar flasks were inoculated with the tenth subculture, and the flasks were incubated for twenty-four hours. The growth was washed off with 0·1 to 0·14 per cent formol saline. The emulsion was filtered and placed in the ice chest till sterile. The antigen was diluted to standard, i.e., 1000 million bacilli per cubic centimetre, and 0·25 per cent carbolic acid added. The end-point of agglutination is expressed as a fraction, the numerator denoting the highest dilution in which agglutination occurred, the denominator being the end-point of the antigen on its homologous antiserum. Our methods for the agglutination reactions were constant, and we followed in certain details the technique recommended by Dreyer. The tubes were incubated at 55° C. for two hours, and the readings taken after half an hour at room temperature.

The *absorption tests* were carried out as follows :—

To one volume of the serum diluted to 1 in 10 with normal saline a creamy, thick emulsion of the absorbing bacillus[11] was added in three doses, i.e., one half and two quarter volumes, at intervals of three hours, and incubated at 55° C., unless otherwise stated. After nine hours the tubes were placed on the ice overnight. The treated emulsions were centrifugalized and the test performed on the supernatant clear fluid. A control saline and serum tube was heated together with the emulsions.

Agglutinin Response of Rabbits to Injections of the Para C Bacillus.

A rabbit was inoculated intravenously with a formol agar vaccine of the para C bacillus, and the response is recorded with the dosage in Table IV.

[11] These emulsions were approximately of the same strength.

TABLE IV.—Intravenous Inoculation of a Rabbit with Formol Agar Vaccine of the Para C Bacillus.

Date of inoculation	Dose	Date of testing serum	End-point of agglutination
21.10.19	100 million	24.10.19	500 20000
24.10.19	250 ,,	26.10.19	10000 20000
30.10.19	500 ,,	3.11.19	20000 20000

This rabbit gave a rapid serum response 20000/20000, that is, to the end-point of the antigen.

This para C antiserum was tested against the stock laboratory antigens, *B. typhosus* and *B. paratyphosus* A, B and C, with the following results: A control tube containing normal human serum and the para C antigen was also observed.

Typhoid antigen and para C antiserum	..	..	0/20000
Para A	,,	,,	,,	..	..	0/20000
Para B	,,	,,	,,	..	..	0/20000
Para C	,,	,,	,,	..	..	20000/20000
Para C	,,	,,	normal serum	..	0/20000

From these results it will be seen that the para C agglutinin is specific, as no reaction occurred with the typhoid or paratyphoid (A or B) antigens.

TABLE V.—Absorption Test. Para C Antiserum 20000/20000, saturated with *B. typhosus* and Paratyphoid Bacilli A, B and C.

Antiserum	Absorbing bacillus	Titre after absorption	Control saline serum
Para C	*B. typhosus*	15000/20000*	20000/20000
,,	*B. para* A	15000/20000*	20000/20000
,,	*B. para* B	15000/20000*	20000/20000
,,	*B. para* C	0/20000	20000/20000

* In all cases 1 in 15000 dilution gave complete agglutination; the end-point was not obtained.

It will be seen from Table V that no absorption of the "C" agglutinins followed the addition of the typhoid and the A and B bacillary emulsions. The effect of absorbing the stock para B antiserum with emulsions of para B and C showed that a B antiserum of 5000/5000 titre was completely desaturated by a para B bacillus, while the para C emulsion removed none of the para B agglutinins.

It will be seen from the above-mentioned experiments that the other members of the enterica group absorbed none of the agglutinins from a para C antiserum of high titre, and that the para C bacillus absorbed none of the agglutinins from this sample of para B antiserum. It is necessary, however, to realize that some para C antigens have a definite B fraction, while apparently a B fraction may develop in a C antigen which was pure when the organism was first isolated.

We conclude that the para B and para C bacilli, although identical in fermentation reactions, are distinct bacteria as judged by serological reactions, as Professor Hirschfeld originally stated.

The agglutinin reactions and absorption tests with a para C antiserum were tested against two strains of Gaertner bacilli and Aertrycke bacilli kindly supplied to us by Colonel S. L. Cummins, A.M.S., with the results shown in Table VI. It will be seen from this table that the paratyphoid C strain has apparently no relationship with the Gaertner or Aertrycke group of bacteria, as in no case was any agglutination or absorption phenomenon observed.

Sir Frederick Andrewes, to whom we are greatly indebted for showing us the results of all his investigations, has found that typical strains of suipestifer and para C are identical serologically. We have tested the *original strain* of para C isolated by Hirschfeld in 1916 with a standard strain of suipestifer furnished by Andrewes. On serological evidence the two strains are identical. Cultural differences with xylose, arabinose and dulcite may occur with some strains of suipestifer and para C. The results obtained by him would appear to us to be of the utmost importance epidemiologically.

TABLE VI.—AGGLUTININ AND ABSORPTION REACTION OF FIVE BACTERIA ON PARA C ANTISERUM.

—	Agglutinin reaction	Absorption reaction
Para C antiserum on—		
Para C bacillus	20000/20000	250/20000
Gaertner, Bainbridge	0/20000	15000*/20000
Gaertner	0/20000	15000*/20000
Aertrycke, Newport	0/20000	15000*/20000
Aertrycke	0/20000	15000*/20000

* The end-point of the reaction was not determined.

THE EFFECTS OF THE INJECTION OF MULTIPLE VACCINES CONTAINING *B. typhosus* AND *B. paratyphosus* A, B AND C INTO RABBITS.

Rabbits were injected with the quadruple vaccine subcutaneously and intravenously, as noted below. Three types of vaccines were employed: (1) heat-killed, (2) formol-killed, and (3) acid dextrose.

From Table VII it will be seen that the agglutinin response was present to each component of the quadruple vaccine when the heat-killed vaccine was employed.

A similar experiment was carried out with the formol-killed vaccine, and in this instance, as in the case with the heat-killed vaccine noted above, a similar rise of agglutinins was noted. The quadruple vaccine was given in doses of 100, 200, 400 and 500 million at six-day intervals, and the agglutinin titre of the serum rose from zero to 1000/8000 with *B. typhosus*,

800/6000 with para A, 800/5000 with para B, and 800/20000 with para C antigens.

TABLE VII.—To show Results of injecting Subcutaneously equally graduated Doses of Heat-killed Vaccines of *B. typhosus* and *B. paratyphosus* A, B and C.

Date of immunization	Dose	Date of testing serum	End-point of agglutination to—			
			T.	A	B	C
5.1.20	100 million ..	5.1.20	0/8000	0/6000	0/5000	0/20000
		8.1.20	0/8000	0/6000	0/5000	0/20000
12.1.20	200 ,, ..	12.1.20	50/8000	50/6000	50/5000	0/20000
19.1.20	500 ,, ..	19.1.20	200/8000	250/6000	400/5000	100/20000
		26.1.20	3000/80000	1000/6000	1500/5000	2000/20000

TABLE VIII.—To show the Results of the Subcutaneous Inoculation of Rabbits with the Quadruple Acid Dextrose Vaccine.

Date of inoculation	Dosage	Date of testing serum	End-point of agglutination to—			
			T.	A	B	C
19.1.20	100 million ..	19.1.20	0/8000	0/6000	0/5000	0/20000
		26.1.20	0/8000	25/6000	0/5000	25/20000
30.1.20	200 ,, ..	30.1.20	25/8000	100/6000	25/5000	100/20000
7.2.20	400 ,, ..	12.2.20	100/8000	100/6000	100/5000	200/20000

A second rabbit was inoculated in this case intravenously with the quadruple acid dextrose vaccine, and the agglutinin response is recorded in Table IX.

TABLE IX.—To show the Immediate and Active Response obtained with Quadruple Acid Dextrose Vaccine when injected intravenously.

Date of inoculation	Dosage	Date of testing serum	End-point of agglutination to—			
			T.	A	B	C
30.1.20	100 million ..	30.1.20	0/8000	0/6000	0/5000	0/20000
7.2.20	200 ,, ..	4.2.20	0/8000	100/6000	100/5000	200/20000
		11.2.20	100/8000	1000/6000	1500/5000	1000/20000

The difference in response is very marked, as shown in these two tables. In nineteen days the acid dextrose vaccine given subcutaneously excited but a feeble response to all four antigens, whereas the same vaccine given intravenously excited in eleven days a marked reaction with the paratyphoid strains, but not with the typhoid.

It was thought that this feeble response to the acid dextrose vaccine

employed subcutaneously might be due to the absence of reaction in the tissues at the site of inoculation. Two further rabbits were inoculated subcutaneously—(a) with acid dextrose vaccine only, while (b) received 0·5 cubic centimetre of ether at the site of inoculation to ensure a tissue response. In Rabbit (a) the agglutinin reactions were again feeble, similar to the previous experiment referred to in Table VIII, while in the case of Rabbit (b) no advantage was obtained by exciting a marked local reaction by means of ether. Rabbit (a) subsequently received two injections of the quadruple formol-killed vaccine subcutaneously and Rabbit (b) one injection of acid dextrose vaccine intravenously, and in both cases a marked reaction to all four antigens occurred.

From these experiments it may be concluded that as an antigen for the preparation of typhoid and paratyphoid (A, B, and C) agglutinating antisera, the heat-killed and formol-killed vaccines are of greater utility than the acid dextrose if the subcutaneous method of inoculation is employed, but the acid dextrose vaccine gives an equally good result if paratyphoid vaccines are injected intravenously.[12]

The Result of the Subcutaneous Inoculation of Man with Paratyphoid C Vaccines.

Over thirty volunteers have been inoculated subcutaneously with paratyphoid C vaccines. The highest agglutinin responses were obtained with the formol-killed vaccines. The inoculation dosage varied in amount, and the resulting serum reactions appeared to have no relationship with the number of bacilli injected. Thus, after a single dose of 250 million of the formol-killed vaccine, a titre of 1500/20000 was obtained; in another instance, although eleven inoculations were given over a period of four months, seven of which contained 1000 million bacilli, the para C agglutinins never rose above 400/20000, while in other cases no reaction occurred. Two healthy men received two injections each of 250 and 500 million of a para C vaccine at an interval of eight days. In one instance the titre of the serum to para C rose from 0 to 1500 in four weeks, while in the other instance no response was effected in the same period. It would appear, therefore, that the agglutinin response to paratyphosus C in any particular individual is uncertain, and may be altogether absent. These findings agree with our observations made on the Serbian soldiers, and on the Bulgarian prisoners in Macedonia.

Agglutination Response to the Inoculation of Formol-killed Paratyphoid C Vaccines.

Twelve men were inoculated with the formol-killed vaccine, and in all but two, in whom no response was excited, a marked agglutination reaction

[12] It must be noted that the para C antigens prepared by us in London were considerably more sensitive than the typhoid and paratyphoid A and B, and that the results of the C agglutinin response must be considered with due regard to this factor.

occurred. Local reactions were noted in a few of these cases. Four cases received a single injection of para C vaccine, and the titres of the sera between the fourteenth and the twenty-first day were 1 in 500, 1 in 800, 1 in 1000, and 1 in 1500 respectively, with an antigen of 1 in 20000 end-point. Three men received two doses of vaccine at intervals of six to eight days, and after fifteen days the response to para C was 1 in 200, 1 in 300, and 1 in 1500 respectively. Of the three remaining cases one received doses of 500 and 750 million, and two 500 and 1000 million, at an interval of seven days, and the titres of the sera for C agglutinins were 1 in 300, 1 in 100, and 1 in 1100 respectively.

From the above experiments, in which formol-killed paratyphoid C vaccines were used, a definite agglutinin response occurred, but the dosage of the vaccine did not correspond to the agglutinin reaction in any way, as one man after three doses failed to respond, while a second, who received a single inoculation of 250 million, gave a reaction of 1 in 1500.

The Inoculation of Men with the Acid Dextrose Vaccine.

The result of subcutaneous inoculation of the acid dextrose vaccine was observed in eleven cases. In no instance was any local reaction observed, and with one exception, in which a slight para C reaction was obtained previous to inoculation, the responses excited were feeble. In the case referred to, doses of 250 and 500 million were given, and at the end of three weeks a reaction of 1 in 1500 was obtained. In two cases in which 250 and 500 million bacilli were injected with a five days' interval, no agglutinin response was obtained, while in eight instances the men received two or more doses varying from 250 to 1000 million, but only a very feeble agglutination reaction occurred.

It would appear, therefore, that the acid dextrose vaccines, when given subcutaneously in man, fail to excite any marked agglutinin response, and these findings are similar to those made in rabbits when this form of vaccine was used subcutaneously.

The Action of Heat on Human and Rabbit Paratyphoid C Agglutinins.

Seven human para C antisera were obtained by the subcutaneous injection of paratyphoid C vaccine. Four of these antisera diluted to 1 in 10 with normal saline gave titres of 1 in 800, 1 in 1000, 1 in 1100, and 1 in 1500 respectively. These sera were heated for nine hours at 55° C, and when re-tested it was found that the end-points had fallen to 1 in 200, 1 in 200, 1 in 25, and 1 in 400 respectively. The three remaining para C antisera, when diluted, were heated at 55° C. for six hours. The end-points of agglutination before heating were 1 in 150, 1 in 300, and 1 in 2000; after heating the end-points had fallen to 1 in 50, 1 in 200, and 1 in 800 respectively. It will be observed that in all cases the paratyphoid C

agglutinins were reduced by heat at 55° C. In one experiment in which a sample of human antiserum was heated at 37° C. for nine hours, a considerable loss of agglutinin content occurred. Two rabbit antisera were heated along with the human antisera at 55° C. for nine hours, but in one case a slight fall from 1 in 25000 to 1 in 20000 occurred, while in the other a fall from 1 in 1500 to 1 in 1250 resulted.

Thus the human paratyphoid C agglutinins appear to be partly thermolabile, while the rabbit para C agglutinin is but slightly affected by heat.

Absorption of Paratyphosus C Agglutinins from Human Sera: Zonular Agglutination.

The sera of four men who had been inoculated subcutaneously with paratyphosus C vaccine, and in whom a good response was excited, were absorbed with emulsion of *B. paratyphosus* C. Before the absorption test was carried out, the titres of the sera were 1 in 800, 1 in 1000, 1 in 1100, and 1 in 1500 respectively. In all four cases complete removal of the paratyphoid C agglutinins resulted, but, as already stated, the thermolability of the para C agglutinins in man must be fully allowed for, as we found that in the serum saline control tubes the titres of the sera had fallen very considerably.

The absorption tests were carried out with two of these antisera at 37° C., instead of 55° C., but it was found that the agglutinins were completely removed, as occurred at the higher temperature.

Zonular agglutination was noted in three of the thirty-five men inoculated with the para C vaccines in London, but was not observed in any of our rabbit antisera. The three human sera above referred to gave agglutination readings as follows:—

(1) 1/25 = 0, 1/50 incomplete, 1/100 to 1/1000 complete, 1/2000 end-point of agglutination.

(2) 1/25 a trace, 1/50 to 1/100 complete, and 1/1000 end-point of agglutination.

(3) 1/10 = 0, 1/25 a trace, 1/50 and 1/100 complete, 1/1000 end-point of agglutination.

This phenomenon, which may give rise to fallacies when human antisera are under investigation, has also been referred to by Macadam[5] while working in Mesopotamia.

The Formation of Paratyphoid B Coagglutinins in the Sera of Persons inoculated with B. Paratyphosus C.

Many of the men who acted as volunteers for these investigations had served in the Army and had been inoculated with the triple enterica vaccine. The sera of these men were tested for the presence of typhoid and paratyphoid agglutinins. As a result of these observations, the men were divided into two groups: (1) those who gave no reaction, and

(2) those in whom a para B response was present with a para B antigen of 1/5000 end-point.

Each group was inoculated with a formol-killed paratyphoid C vaccine with doses varying from 250 to 1000 million, and as a result it was found that some men of both groups showed a definite rise in the titre of the para B agglutinins, while others failed to respond. This para B agglutinin response was not dependent upon the amount of paratyphoid C vaccine injected.

Para C Infection in London.

In March, 1920, the *B. paratyphosus* C was grown in blood culture from a case of enterica admitted at St. Thomas's Hospital. On March 18 a girl (M. N.), aged 12, was admitted under the care of Dr. C. R. Box, who has kindly permitted us to publish the following notes :—

The patient had been ill for two days, suffering from headache, vomiting, and general malaise. She had a rigor immediately preceding admission. On admission the temperature was 102° F., and the pulse 112. No spots were seen. The spleen was enlarged and palpable. On March 21 the temperature reached 104° and the patient was delirious. Pulse 132. Epistaxis occurred. The temperature lasted for six days after admission, and then fell to subnormal and remained so throughout convalescence. Bowels were constipated throughout. A blood culture was made on March 22, and the serum was also collected. The blood culture in distilled water grew a Gram-negative motile bacillus, which gave the cultural reactions after seven days' incubation of the B and C bacillus.

The serum was tested on March 22 and 29 and April 9. On the first occasion against *B. typhosus* and *B. paratyphosus* A and B no agglutination occurred. The para C reaction was also tested on the second and third occasions, but no reaction was obtained. This bacillus was not agglutinated by the patient's serum, and when tested with the stock typhoid and paratyphoid A, B and C antisera gave the following results : T = O, A = O, B = 400/5000, and C = 2000/2000. The fæces were examined on four occasions, but the para C bacillus was not recovered. No history was obtained of any relative having been in the East. The father, a soldier, had been in France, but had never suffered from any enterica-like infection.

Sir Frederick Andrewes has very kindly informed us of a case of para C infection which occurred at St. Bartholomew's Hospital in 1919 in a man who had been in Mesopotamia. The organism was obtained by blood culture and from the urine. The case, however, was *not* enterica on clinical evidence.

In conclusion, we offer our thanks to Professor Hirschfeld, who supplied us with the original strain of the *B. paratyphosus* C in 1916, and to our various colleagues in the Balkans who assisted us with our observations, more especially to Captains W. J. Deadman and J. Anderson, R.A.M.C.

MEDICAL HISTORY OF TRANS-CAUCASIA IN SO FAR AS IT AFFECTS AN ARMY IN THE FIELD.

By Lieutenant-Colonel P. H. HENDERSON, D.S.O.
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Climate.

As the climate of Trans-Caucasia varies considerably in different areas, it will be most convenient to consider separately (*a*) the Black Sea Basin, (*b*) the Armenian Highlands and (*c*) the Caspian Basin.

(*a*) *Black Sea Basin.*—In this part of the country, which includes the area west of the Suram Mountains, the climate is characterized by a moist atmosphere and a moderate temperature, the mean annual being approximately 60° F., with mean variations of about 42° F. in January, 63° F. in May, and 77° F. in August. The annual rainfall varies considerably in different districts in this area, reaching as high as 80 inches in Batum, 65 in Poti, and between 40 and 50 in Kutais and Sukhum.

The prevailing wind varies in different districts, being S.E. in winter, except at Kutais, where it is N.E. In summer it is N.W. in Batum, W.N.W. in Kutais, S.W. by N. in Poti, and S.W. in Sukhum.

The winter is mild, and though snow falls it rarely lies. The coldest period is from the middle of January to the middle of March, strong gales being common during these two months.

The summer is hot and muggy. Vegetation is luxuriant, and near the sea tropical, subtropical and temperate varieties are to be found.

(*b*) *The Armenian Highlands (include Alexandropol, Araliki, Erivan and Shusha).*—In this area one meets with climatic conditions somewhat similar to those met with in the other two, but, in addition, one finds here extremes of cold and heat, snow lying in several parts of the area till the middle of April. Spring is very short, lasting about a fortnight to three weeks, and is followed by a hot, dry summer which parches the country.

The mean annual temperature is approximately 50° F. with mean variations of about 19° F. in January, 60° F. in March and 73° F. in August. The mean temperature of Alexandropol district is however considerably below the mean for the area, reaching as low as 13° F. in January and only rising as high as 66° F. in August.

The average annual rainfall is about fourteen inches. The prevailing wind varies very considerably in the different districts.

(*c*) *The Caspian Basin* includes the area east of the Suram Mountains and comprises the districts of Baku, Leukoran, Tiflis and Temir Khan Shura. In this area the climate is, on the whole, dry and extremes of heat and cold are met with. The heat is most oppressive in the Kura Valley. In Baku sand and dust storms are common and after a heavy rainfall the streets and main drains are frequently silted up with sand and debris. The

mean annual temperature is about 56° F., with mean variations of approximately 34° F. in January, 65° F. in May and 76° F. in August. The average annual rainfall approaches eighteen inches. The direction of the wind varies greatly in the different districts.

Clothing.

Khaki serge is the most suitable uniform for eight months of the year. Drill uniform with shorts, the latter having prolongations for turning down at dusk, to prevent mosquitoes from biting, is recommended from May to the end of August. In several hill posts, however, it is necessary to put on serge in the evening even in summer. Helmets are not essential in summer if slouch hats are available. During our occupation they were worn during the three hottest months from about 9 a.m. till sunset.

Sanitary Conditions.

Although sanitary conditions as a whole are very much below the standard one meets with in Great Britain, there was evidence that a considerable advance had been made by intelligent Russians during the years preceding the Revolution of 1917, and an attempt had been made to introduce modern sanitary methods into the towns in Trans-Caucasia. Certain war sanitary appliances in the form of bathing and disinfecting trains, small portable steam disinfectors and bathing establishments comprising Russian steam and shower baths, were in advance of any similar appliances I have seen introduced for the British Army in the field. The huts forming the hutted hospitals in Batum, and certain of the ambulance coaches on the ambulance trains, particularly the bathing, cooking and dispensary coaches, were also superior to any I have met with in other theatres of war.

The bathing and disinfecting trains were capable of dealing with 600-800 men per day. Two such, made I believe in England, and presented by wealthy Armenians to the Imperial Russian Army, were taken over by the Division, but after we had placed the necessary sanitary personnel on board and put everything in working order the Georgian authorities suddenly removed the trains during the night to an unknown destination, and the British personnel had to make a hurried exit to avoid being carried away. The trains were made up of several coaches and contained an undressing room leading to the bathrooms, which were fitted with hot sprays. The bathrooms in turn led into a dressing room, where clean clothing was issued from linen and clothing stores. Here, if necessary, men could sit and wait till certain articles of clothing which might be required were disinfected, and they could have coffee if desired.

The dirty clothing was passed through a very large and efficient steam disinfector capable of registering over thirty pounds of pressure. There was also a vapour disinfector for dealing with special articles of clothing. After disinfection washable articles were passed to the laundry coaches where they were washed, ironed, and returned to clean stores for re-issue. There

were also comfortable living quarters for the personnel of the train. The value of such trains which could follow up advancing troops, wherever a railway was intact, is inestimable.

The small portable steam and vapour disinfectors were a great improvement on the British Army "Thresh," as the former were light and easily drawn by one horse or mule while the latter is extremely cumbersome and difficult to transport.

The Russian steam bath followed by a shower is ideal as a means of cleansing the body.

Water Supplies.

Practically all the towns and villages are well supplied. Baku and Batum received piped supplies of upland service water of good quality and ample in quantity. Tiflis, on the other hand, is badly served both as regards quantity and quality. About two-thirds of its supply comes from the polluted Kura River, while the remaining third—obtained from a catchment area in the mountains—is of good quality. Purification is incomplete and unsatisfactory, and as the water from the purer source is mixed with that from the Kura River all the water delivered in the mains is unsafe for drinking purposes. In pre-war days and in the earlier phases of the war the river water was led by an aqueduct to settling tanks where it was treated with alum in order to precipitate suspended matters. From these tanks about half of it was then passed through sand filters and finally all three supplies, i.e., the comparatively pure but untreated upland surface water, the filtered river water and the river water after sedimentation, flowed into a common aqueduct to the pumping station where it was pumped into the mains.

During our occupation of the Caucasus both sedimentation and filtering plants were out of action and in addition only three out of seven pumps were working and these three were in a precarious condition. In consequence we had to adopt local means of clarification and sterilization. Each unit improvising its own filter of four-ply blankets on a wooden frame, the water being treated with alum. The filtered water was ultimately sterilized with bleaching powder.

From early spring when the snows begin to melt until the middle of summer, the Kura River is of good volume but the water is brown in colour and somewhat resembles coffee grounds, and during our occupation it was delivered in this condition from the pipes. In late summer and autumn the volume rapidly decreases and it becomes comparatively clear. The supply during this period is insufficient for the town and the practice is for the supply to be cut off from one half of the town during the forenoon and from the other half during the afternoon.

During this period, and also during the spring and early summer, units supplemented their drinking and cooking supplies from mountain springs water mules with pakhals being sent out daily for this purpose.

During winter, when more rain falls, a more ample supply of fairly clear water is available.

Disposal of Excreta.

The water carriage system is found in the larger towns, but the sewers usually discharge the raw sewage direct into the sea or a river.

In Batum all w.c.'s discharge into cesspools, of which there were over two thousand in the town. These are periodically emptied by means of tank lorries with lift and force pumps, or by tank carts with hand ladles. Part of the night soil is then disposed of about one mile to the east of the town through an opening in a concrete platform which connects up with a drain discharging into the Black Sea. The remainder, prior to our occupation, was dumped into a pond in close proximity to the Barracks on the west side of the town. On our arrival in December, 1918, it was found that the Turks had dismantled most of the lorries and carts, with the result that the cesspits were overflowing into the streets and gardens, and it was a considerable time before the lorries and carts could be repaired and the appalling state of insanitation improved.

In Baku the main sewers are frequently blocked by sand after rain storms.

Refuse.

This was usually disposed of by dumping it into a stream or into the sea, or more commonly on a refuse heap in the vicinity of the town or village.

Cleanliness.

Although bathing facilities are in many places very good, the poorer classes are as a whole dirty and frequently verminous. To cope with this, good steam disinfecting and disinfestation plants had been established in most towns, and large numbers of smaller portable steam and vapour disinfectors were also to be found.

Storm Water Drainage.

Although the drainage in the towns is usually good, marshy areas in which mosquitoes breed freely were met with to the west of Batum, at Petrovsk, the Terter Marshes near Shusha, and along the valley of the Kura.

Prevailing Diseases.

The most important prevailing diseases met with were malaria (malignant and benign), typhus fever, small-pox, relapsing fever, dysentery, cholera, enterica, and the three varieties of venereal disease. Malaria usually first appears in June, reaches its maximum in August and dies off about October 10. The malignant type is most commonly met with during the last two months of the malarial season. The malaria-bearing mosquitoes met with were *Anopheles maculipennis*, *A. superpictus* and *A. bifurcatus*,

although no doubt other species also existed. The most malarious areas in our occupation were Batum, particularly to the west of the town by the aerodrome and Ardaham Barracks (practically the whole of the Royal Air Force stationed here were infected), the marshy area on the banks of the Terter where the Berkshire Regiment was severely infected, and Petrovsk. Baku was comparatively free, and also Tiflis with the exception of houses situated close to the Kura River.

Typhus fever was very prevalent amongst the civil population owing to the verminous condition of the poorer people. The prisoners in the civil jails also suffered severely in consequence of the insanitary conditions under which they were compelled to live, no opportunity being afforded them of freeing themselves from vermin. There were comparatively few cases amongst the British garrison, but the death-rate was high.

Small-pox was fairly prevalent owing perhaps to a shortage of vaccine lymph amongst the civil population. About twelve cases occurred in the British garrison.

Dysentery was very common in the civil population.

In view of the insanitary surroundings and the consequent prevalence of flies and the very bad water supply at Tiflis it was thought that the British garrison might also suffer, but fortunately very few cases occurred.

Cholera occurs annually amongst the civil population throughout Trans-Caucasia and not infrequently assumes epidemic form. Special cholera hospitals are to be found in Baku and Batum. Although cases were common amongst the civil inhabitants during our occupation the British garrison escaped infection.

Venereal diseases were the chief source of inefficiency, all three varieties being commonly met with. A large majority of the prostitutes appeared to be infected. Prophylaxis with potassium permanganate, calomel cream, etc., was of definite value where intelligently and efficiently carried out.

The other prevailing diseases were less common. A considerable number of the troops in the Armenian Highlands suffered from snow blindness, necessitating the issue of smoked glasses.

Oriental sore is fairly common amongst the inhabitants, and the carrier of the infection is thought by many local doctors to be stomoxys.

British Sanitary Organization.

The country was divided into three sanitary districts, Baku, Tiflis and Batum, each under a sanitary officer who had at his disposal a sanitary section or portion thereof. Outlying posts were allotted to districts according to proximity and means of access.

Medical Arrangements, Hospital Accommodation.

Suitable buildings were acquired in all the towns occupied by the British. The only difficulty experienced was in Tiflis, where a stationary hospital and two field ambulances had to be accommodated. The Georgians

at first put many obstacles in our way and did their utmost to prevent us from obtaining suitable buildings, but eventually these medical units were established in a Georgian college, a seminary and a school, all well adapted for use as hospitals.

One field ambulance was converted into a venereal hospital of 200 beds, the other into a 200-bedded infectious diseases hospital for all infectious diseases except dysentery, the stationary hospital of 600 beds receiving all other cases. In Baku the hospital accommodation consisted of one field ambulance of 200 beds acting as a hospital for all infectious diseases except dysentery, and a casualty clearing station of 500 beds which received all other cases. The field ambulance was established in a school and the casualty clearing station in a large seminary which had previously been used as a hospital by the Russians.

In Batum the hospital accommodation consisted of a stationary hospital, a casualty clearing station and a field ambulance. The stationary hospital was established in Russian barracks which had been converted into a hospital by the Russians early in the war. It provided excellent accommodation for 600 patients and had two good operating theatres, one for septic and one for non-septic cases. All infectious cases were admitted here and also general, medical and surgical cases. It was well suited for this purpose as it consisted of a number of separate pavilions and also had a good officers' pavilion consisting of a general ward and one or two bunks. The sisters were accommodated in charming cottages, one of which was set aside as a sisters' hospital of seven beds. The casualty clearing station (450 beds) was accommodated in a Russian hutted hospital. The huts were well constructed and admirably equipped with operating theatres and sanitary annexes. General, medical and surgical cases were admitted here. The field ambulance of 200 beds was established in huts similar to those of the casualty clearing station and acted entirely as a venereal hospital.

When Indian troops were added to the British garrison most of these medical units were provided with an Indian section.

At Krasnovodsk half an Indian section of a field ambulance was established in a school which provided good accommodation.

At Kars a section of an Indian field ambulance was opened in a suitable building. Smaller medical posts, British and Indian, were also established at Shusha, Borjom, Akhaltsikh, Erivan, Ararat, Nakhitchevan, Artvin, Gagri, and many other posts held by British and Indian troops. The long distances separating these posts put a severe tax on the medical personnel and transport.

Medical and Surgical Stores.

These were supplied from an advanced depot of medical stores well situated in a commodious stone building in Batum railway station. This advanced depot in turn received its supplies from a base depot at Constantinople.

Laboratories.

One laboratory was established in the casualty clearing station at Baku and one in the stationary hospital at Batum and did excellent work in the diagnosis of malaria, typhus, relapsing fever, etc.

Dental Centres.

Dental centres were established at Baku, Tiflis and Batum.

Medical Transport.

From Enzeli (N. Persia) and from Krasnovodsk (Trans-Caspia) cases were transported in reserved cabins in the ordinary passenger ships, medical personnel being provided from the medical units in Baku, as and when required.

A captured Bolshevik hospital ship with accommodation for twenty-five lying cases was about to be taken into use for this purpose and also for the evacuation of naval casualties in the Caspian, but owing to the decision to evacuate Trans-Caucasia the project was abandoned.

From Petrovsk casualties were evacuated to Baku in two ambulance coaches with a kitchen coach attached to passenger trains—personnel for the care of the sick being provided from the medical post at Petrovsk where the coaches were kept when not in use.

From Shusha cases were brought in Ford ambulance cars to a post on the Baku-Tiflis-Batum Railway whence they were transferred to the ambulance train. An excellent Russian ambulance train, with accommodation for 150 cases and provided with kitchen, dispensary and administrative coaches, and equipment and stores vans, was taken from the Turks on our arrival, and evacuated British and Indian casualties from Baku and Tiflis to Batum. The journey in peace time occupies about twenty-seven hours but the railway had become so disorganized that the average journey took three to five days. The usual British and Indian personnel for an ambulance train was provided as a separate unit. A proportion of these carried rifles to ward off the attacks of local inhabitants and to prevent them from pillaging the train.

From Kars and other outlying posts on the railway cases were brought to Tiflis in ambulance coaches similar to those at Petrovsk.

Casualties from outposts in the Armenian Highlands were brought to railway posts by sleighs, travois, litters, riding mules, ambulance wagons and cars. From one outpost the only suitable transport was a sleigh and the journey occupied about five days.

From Poti, Sochi and Gagri on the Black Sea minor casualties were transported to Batum in the ration boat, severe cases being brought in on a destroyer.

Generally speaking good roads suitable for ambulance cars and wagons are few and are confined to the vicinity of towns and villages. There are, however, a few first-class military roads. In consequence of this the cars

of the motor ambulance convoy were distributed to posts where they could be utilized—wagons, litters and travois being used where the roads were bad.

Were it necessary to carry out active operations in the interior of the country, travois, litters, sleighs and riding mules would form an essential part of the ambulance transport.

Hospital Ships.

These were sent from Constantinople to Batum when required and patients were evacuated by them to Constantinople or direct to England according to the nature and degree of their disabilities.

Civil Hospital Accommodation.

There were several well equipped hospitals in each of the main towns, Baku, Erivan, Tiflis and Batum, but there was a great shortage of drugs, surgical dressings, vaccines and sera.

Rations.

Local beef, which consisted chiefly of trek ox and buffalo, was unfit for rations. Local mutton was of better quality but was much inferior to British or Australian mutton.

For a considerable time after our arrival, owing to the want of a ship containing cold storage and the absence of similar arrangements on the trains, the local fresh meat ration was very poor and bully beef was issued for a prolonged period.

The country abounds in all varieties of fruit, and fresh green vegetables are also easily obtainable, potatoes are not abundant. After a considerable time our onion and dry vegetable ration was supplemented by local purchase of fresh fruit and vegetables.

Scurvy did not occur amongst the British garrison but about a dozen cases were found amongst the troops which arrived from Mesopotamia.

RANDOM NOTES ON FIELD MEDICAL UNITS.

By Major (Brevet Lieutenant-Colonel) G. W. G. HUGHES, D.S.O.
Royal Army Medical Corps.

The Journal of the Royal Army Medical Corps welcomes notes on the experiences of officers during the war. I have been looking in vain for such in the Journals lately. That there are dozens of men more fit than I to suggest and criticize, I know. It is with the hope that these random, rather disjointed notes may stimulate others to write too, that I venture, with a good deal of diffidence, to make my first contribution to our Journal. Could we not get some officers from outside the corps that have been in the Infantry, or on Brigade or Divisional Staffs, to give us their criticisms and suggestions on the work of the Royal Army Medical Corps in war (and in peace for that matter). It is salutary, too, to hear from patients, officers and men, their experiences in hospital, motor ambulance, train and ship. The officer who wrote complaining of being given an aperient, but so quickly was he transferred from one medical unit to another that he had never sufficient opportunity to attend the results, really did good in arousing sympathy in even our hard breasts.

It is interesting to look back to the years before the War and to try and remember what were one's ideas of Royal Army Medical Corps work in action. I remember being at a training camp on Salisbury Plain. We had schemes for collecting wounded, picking them up from all over the country, carrying them back over the open to the horsed ambulances. At night we used bull's-eye lanterns to find the wounded. Our dressing-stations were on nice open sites, preferably near cross-roads. The chief feature of the dressing-stations was the operating tent and we were proud of the operating table, the anæsthetics laid out ready and the acetylene operating lamp, all ready for work. Our accommodation for wounded was a few bell-tents.

What field ambulance, during the War, ever used its operating tent as an operating tent? Imagine the excitement at night if a brilliantly-lighted tent were pitched within the mile or so of the front line that we considered the main dressing station should be!

And yet that training was most useful. I had before only the vaguest idea what a field ambulance was. The whole army had to learn many bitter lessons in the arts of taking cover, avoidance of shell-fire and bombs, the difficulties of transport, the numbers of wounded and other casualties, and so on and so on almost *ad infinitum*.

We have learnt much. Probably these lessons will be acted on and new mobilization tables, etc., may be already made out—and the next war may be so different from this last one that even the new scheme may be too old. However, I have endeavoured in these notes to give what are at least some bases for discussion.

Organization.

In suggesting any new organization of field medical units one is at once "up against" the difficulty of catering for mobile and for stationary warfare. However, modern shell-fire inevitably means elaborate trenches, and trenches are easy to defend and difficult to take, and consequently it would seem that there must be periods of stationary warfare. It is during stationary warfare that there is time for the staffs to tackle the problems of keeping up the strength in numbers of the fighting troops, or preventing wastage as far as possible.

Returns of the sick and the wounded are examined, and it is soon realized that there are many trivial cases which, being unfit for duty, are being lost to the divisions. So a rest station is formed. If there are many scabies cases a special station for that is made. Casualty clearing stations are implored to send as many cases back to duty as possible. This means that casualty clearing stations must enlarge their accommodation.

A man is on the strength of his division until he leaves the Army area, i.e., until he is put into an ambulance train. The Army, the corps, the division, all do their utmost to prevent men getting down the line of communication. This is in many ways very praiseworthy, but there are many drawbacks. To take the point of view of the Assistant Director of Medical Services of a corps. It has often been found economical to form corps main dressing stations, walking wounded collecting posts, posts for gassed cases, rest stations, scabies stations. He has also often been required to provide personnel to assist the casualty clearing stations. In his corps divisions go into the line, come out to rest, join the corps and leave it. Consequently he has constantly to make arrangements for the changing of personnel at his various corps' medical units. This is not only difficult and troublesome, but is bad for the efficiency of the various concerns. It would seem that corps, like divisions, should have some medical units on their establishments. As it is none of the corps medical units is mobile. Field ambulances provide some of the equipment, but—for instance, in a rest station—there are tents or huts, baths, kitchens and equipment that have been provided from Heaven knows where. These corps medical units were very successful and economical. The front held by a division may be very much narrower than was considered probable before the War, and it would often be absurd for each division to have its own main dressing station. A corps had 3, 4 or more divisions, each division with 3 field ambulances each with their 3 bearer and tent subdivisions. It never happened to me, and it must very seldom have happened to any field ambulance that the whole equipment was in use. I have known of divisions which dumped the equipment of at least one section of each field ambulance before going into the line. There is here an obvious possibility of economy in divisional medical equipment and transport which might be given to the corps.

Where these corps medical units were in existence all that a division

was responsible for was the evacuation of the wounded to the main dressing station, the formation of an advanced dressing station, and of the necessary regimental aid posts and bearer posts. So all that was needed by the division was more or less the old "bearer company," which is a far more mobile unit than a field ambulance, requiring no more than a third of the equipment and transport.

Field ambulances are "divisional troops," and under the direct command of the Assistant Director of Medical Services. I have known divisions where this was very much insisted on, and the idea of a brigadier inspecting a field ambulance much resented. But I am sure that when a field ambulance is attached to a brigade, and, as far as possible, stays with it, there is, as a rule, a very much better feeling towards the Royal Army Medical Corps without any interference with the powers of the Assistant Director of Medical Services than if it were kept aloof. I have very great cause to be profoundly grateful to the brigadiers and their staffs that I have worked with for their many kindnesses and real help. We were proud of our brigade, and, I think, the brigade were not ashamed of us. Of course it often happened that we were separated as might be a field company of Royal Engineers, but when our detached duty was over we returned to our brigade.

Casualty clearing stations were Army troops and directly under the Director of Medical Services. In one Army at least the casualty clearing stations were distributed amongst the corps. Just as with field ambulances and brigades this scheme was undoubtedly a success. It was always possible for the Director of Medical Services to detail a casualty clearing station to receive wounded from any other corps, but the interest taken by the corps commander in his own hospitals was most beneficial, and, too, I think it tended to break through what was apt to be a rather marked line of demarcation between the casualty clearing station and the field ambulance.

Motor Ambulances.

I remember the first motor ambulances coming out. One car per division was regarded as magnificent. We had always been told, before the War, that the War Office had ruled motors for the medical services as out of the question, that the transport of a division was too large as it was, that motor vehicles could not travel at the same rate as horsed transport, and so on. It is probable that motor transport will largely replace horsed transport in future. It must be more economical in the end. It is to be hoped that a standard pattern of motor ambulance will be devised. There were Fords, Daimlers, Sunbeams, Talbots, Wolseleys, etc., each with its different spare parts. What was wanted by divisions was a car a little stronger and better sprung than the Ford, but not so clumsy as the larger cars. The body hung always too far behind the back axle; the inside sucked in dust and petrol fumes. A heavier type of car could be used for convoys on the better roads.

Returns, etc.

One often wondered whether any notice was ever taken of some of the returns we had to send in. Daily states, weekly states, trench feet returns (with countless questions to be asked from each man). Returns of gassed cases, venereal and scabies, albuminuria and nephritis, drugs issued to Portuguese and to civilians, etc., etc. There should be a limit to the number of these returns—and we were told to economize in paper!

Quite rightly, the most important record in any medical unit is the A. and D. Book, but it might be improved on. I remember being shocked to find that badly wounded men, suffering agonies of pain, were being pestered to give their total service in months, service in France as well as many other details. We found a rough A. and D. Book at the advanced dressing station very useful.

In all medical units it is a common experience to be asked questions about patients who were in hospital, perhaps, some years ago. As a rule, it is in cases of deaths in hospital. Relations living, perhaps in the colonies, write wanting to know as many details as possible: what he said, whether he was conscious, in pain, etc., etc. The sisters get the same kind of letter, and so do the padres. Even if the officers, padres, and sisters were not constantly changing, it would be difficult enough to answer these letters—sad, touching letters most of them are. The best system is to get the padres to keep an unofficial record of all deaths or dangerously ill cases with as many personal notes as possible gleaned from doctors, sisters, and orderlies, as well as from the patient himself. This record should be kept in the unit.

Then there are the many inquiries after lost kits. We all know how all deficiencies were put down to the predatory habits of the Royal Army Medical Corps. We know how seldom this was deserved, but that it was occasionally deserved we also know. And it is always in times of "pushes" that it is most difficult to keep check. Still, lists of small valuables, field glasses, revolvers, etc., must be made *as early as possible* for every helpless case. The credit of the unit and the corps makes this a necessity.

Equipment.

I suppose all units, especially the mobile ones, such as field ambulances, soon realized that much of their equipment was unnecessary, and wisely handed in what they could dispense with. There was a good deal that could be dispensed with. But there was also much equipment that one had to carry that was not according to scale. I have known field ambulance transport having to do double journeys because of all sorts of extra stores—wood for buildings, extra blankets, extra clothing for gassed cases, extra tentage. Casualty clearing stations, when made to move, had an extraordinary quantity of extra equipment—Red Cross stores, beds, tent-bottoms, etc.

What of all this was unnecessary, and what indispensable is a matter of opinion, but certainly there is much scope for revision of existing, or, rather, pre-war scales. To take tentage as an instance—I never saw the bell-tents of a field ambulance used for anything but for billets for the personnel, and for this purpose they were often an absolute necessity. It is well known, too, that the present small hospital marquee is not economical in the space it takes up and in weight compared with the accommodation it provides. The French hangar pattern is very much better.

Then as to Red Cross stores—quite apart from the luxuries such as the red blankets, the counterpanes, the gramophones, playing cards, games, cigarettes, sweets, etc., which were so generously provided, there were many things really necessary that could only be obtained from the Red Cross. This was almost unavoidable. Nobody could deny that the Army Medical and Ordnance Stores did wonderfully well in catering for the constantly altering conditions and requirements during the War. But still an examination of the lists of articles supplied to units by the Red Cross would be a most useful guide when revising equipments.

Then there were the gifts from local societies and private individuals. Many of us have experienced the dismay when told that a large box of woollen goods has arrived in mid-summer or a huge crate of moss dressings has been dumped on us when the transport was already fully loaded.

But luxuries are, under some conditions, necessaries. The difference between a bright, cheery-looking hospital or rest-station and a comfortless, stretcher-floored tent or hut to a sick or wounded war-weary man is obviously great enough to make luxuries well worth the extra trouble they cause. We need in the Army, in war and in peace, a department for the supply of such "extras," not only for medical units but for all the Army. I cannot tell if the Red Cross Society was wasteful in money. I think it must have been. But its results were splendid. I hardly can realize what we would have done without it.

Personnel.

I have many a time heard discussions on the necessity for the regimental medical officer. There is absolutely no doubt that a good regimental medical officer is, in the end, an economy. He saves wastage of men from sickness, trench-feet, gas, besides attending to the wounded and organizing the regimental stretcher bearers. His presence with the officers and men is a help not only to them but to the Assistant Director of Medical Services. It is true that there is little professional work to do, and that an intelligent N.C.O. might do that little equally well, but I am sure that the presence of an officer who is a doctor and a gentleman provides an invaluable liaison between the troops and the Royal Army Medical Corps, and is largely responsible for the success we have every

reason to be proud of, and for such popularity in the Army as we have earned. At the same time I think the regimental medical officer need not be cut off from the field ambulance, or the bearer company that I have already spoken in favour of.

I do not see why the regimental stretcher bearers should not be Royal Army Medical Corps. I would make them also part of the bearer company. The evacuation of wounded would be smoother, there would be no possibility of doubt as to the zones of work of the regimental and field ambulance bearers, and regular reliefs and replacement of casualties would be more easily arranged. There is surely no need to impress on any one in our corps that stretcher bearers must be of as good physique as any of the Infantry.

Padres.

Field ambulance commanders must often have ardently wished that the reunion of Christendom had come about before the War, when just before a "push" one was beset by Church of England, Roman Catholic, and Nonconformist padres, who wanted accommodation in already cramped mess and billets, or dug-outs. Not that they were not, almost always, really good fellows, anxious to help and often really helpful, but they were sometimes *de trop*. I remember on one occasion suggesting that three padres of different persuasions should, with their batmen, dig their own dug-outs near an advanced dressing-station and mess together, and finding the idea meet with no enthusiasm. I do not see why they should not be trained in nursing duties, certainly in First-Aid. They would welcome the idea, I know, because I once did lecture the padres of a division at their request, and they were really keen to know how to help.

That there are many important points untouched on in these Notes I fully realize. Already I find that I am forgetting many of the details, the problems which we all had to tackle during the last War. When the next war will be and what type it will take is impossible to forecast. In an article in the *Times* I read: "In the next war chemical warfare will play a decisive part; that appears to be certain." How can we prepare for this? What differences will that make to our organization and equipment Such are the questions that we must all endeavour to answer.

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CARBON MONOXIDE POISONING IN WARFARE.

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Part I.

In addition to poisoning by the various "drift gases" and "shell gas" fluids made use of by the enemy, there is another very important type of gas-poisoning met with in warfare.[1] This is poisoning by carbon monoxide, "mine-gas poisoning" as it is called to distinguish it from the drift-gas poisonings; and it is usually met with among men of the engineer units engaged in the mining and countermining, that of necessity accompanies stationary warfare, and has done so at least since the days of Herodotus and Josephus.

The carbon monoxide, which has been described by Brouardel as holding first place amongst the toxic gases (*Les Asphyxies par les Gaz, les Vapeurs et les Anesthésiques*, 1896, p. 5), and which is the toxic agent in these cases, is produced during the explosion of the charges in the mines, and is evolved in such quantity that in the case of a mine exploded in the month of September, 1916, the gas, issuing from the ground broken by the explosion, and taking fire, burned with a flame visible at a distance of a mile, and had not entirely ceased to burn at a quarter past four in the morning, five and three-quarter hours after the mine had gone up. Where the mine is more deeply placed or where a smaller charge has been used, so that the surface of the ground has not been broken, the gas is either forced into the underground system of mine galleries or gradually percolates into the galleries through cracks and porosities in the ground, and in these circumstances the miners become subject to this form of gas-poisoning, the severity of which may range from mere headache and debility to coma and death. Both among the Germans and among our own men many casualties have occurred in this way.

In some cases the reflux of carbon monoxide after an explosion has come up the mine-shaft and caused gas-poisoning in persons in the trench in the near vicinity to the mine entrance. There is a persistent rumour, too, that during the first winter of trench warfare (and certainly such cases occurred during every subsequent winter of the war) there were cases of carbon-monoxide poisoning with some fatalities apart from mining work, due to braziers of burning fuel having been taken into dug-outs during the night, the dug-outs having been sheltered against the bitterness of the winter cold by a heavy blanket hung across the entrance and

[1] In Penhallow's "Military Surgery" (1916) the only forms of gas poisoning mentioned are shell gas and drift gas.

effectually preventing the escape of the products of combustion; carbon monoxide, as is well known, having even in relatively small quantities the effects of a cumulative poison, although it is not possible to go as far as Claude Bernard and say that every breath drawn in an atmosphere containing this gas kills a certain number of blood corpuscles until they are all dead and respiratory exchange is no longer possible. The vast majority of cases of carbon-monoxide poisoning among soldiers, however, is true mine-gas poisoning in the literal sense and occurs underground, the victims being almost exclusively drawn from those working in tunnelling and other duties connected with underground warfare. The case immediately cited is an example of gas-poisoning where the gas had welled up the shaft of the mine, although the patient was not actually in the open air at the time he was gassed.

J.M., aged 22, eight days ago was gassed with carbon monoxide while he was in the sloping gallery leading to the head of the shaft at the time a small mine was exploded. The gas welled up the shaft, reaching the place where he was waiting. He became dizzy and weak, and came out into the open air; he has continued to feel "fair beat" ever since, with slight looseness of the bowels from time to time.

The problems of gas poisoning in mining operations in the chalk are quite different from those encountered in working in a clay stratum, owing to the presence of fissures in the former and its porosity to gas, which may be retained for comparatively long periods and afterwards forced out into the workings by changes in barometric pressure, or by a rising water-level in the chalk.

As has just been stated, the carbon monoxide which is the toxic agent in these cases is engendered by the explosives in use in the mining operations, and is liberated in relatively large amounts.

The various explosive substances contain within themselves a considerable amount of oxygen (with certain exceptions, such as the acetylene compounds), which is, however, generally insufficient for the complete oxidation of all the constituent oxidizable elements.

In consequence, not only may there be the formation of carbon monoxide, but hydrogen, marsh gas and certain other oxidizable substances may be liberated as the result of the detonation of various explosives. The methane is said to result from interaction of the hydrogen with the oxides of carbon as the hot gases cool down, and not to be formed at the time of the explosion. Nitroglycerine is an example of the explosives which are completely oxidized on detonation, and this substance exists to the extent of seventy-five per cent in dynamite, and thirty per cent in cordite, besides being present in smaller proportions in many of the blasting gelatines. Its detonation may be expressed by the following formula:—

$$4C_3H_5(NO_3)_3 = 12CO_2 + 10H_2O + 6N_2 + O_2$$

Although it is capable in the presence of a suitable absorbent, such as

exists in dynamite, of burning slowly in air from which it absorbs still further oxygen with the formation of the higher oxides of nitrogen. The gases evolved from the ordinary detonation of nitroglycerine are sufficiently copious to give from one kilogramme of the explosive 713 litres of gas at N.T.P. when the water vapour has been condensed out. These gases, however, contain no carbon monoxide, although the oxides of nitrogen resulting from the imperfect detonation of a charge of dynamite are extremely pernicious in their effects if they happen to be inhaled.

Carbon monoxide is produced as the result of the use of a large series of explosives, such as gunpowder (whether in the form of rifle powder, "cocoa powder," or blasting powder), guncotton (either by itself, or as cordite, of which it forms 65 per cent); smokeless powder, which is 98 per cent guncotton with 1 per cent of acetone and 1 per cent of moisture, etc., or the blasting gelatines, and ammonal, the latter of which is used extensively and in enormous quantities, charges being laid and exploded such as had never been heard of or even imagined in times of peace. The fulminate in the detonators also liberates CO, but owing to the relatively small amount of this substance that is necessary, this factor may be ignored. The formula for the decomposition of the fulminate in the detonators is as follows :—

$$HgC_2N_2O_2 = Hg + 2CO + N_2;$$

sixty-six per cent by volume of the small amount of gas liberated consisting of carbon monoxide, not, however, at the instant of detonation, as the molecular mercury liberated occurs momentarily in gaseous form also. The greyish fume given off on explosion of mercuric fulminate consists of finely divided metallic globules condensing out from the rapidly cooling gas.

A typical formula for the explosion of a charge of gunpowder may be given as under :—

$$21C + 7S + 16KNO_3 = 13CO_2 + 3CO + 8N_2 + 5K_2CO_3 + K_2SO_4 + 2K_2S_3;$$

12½ per cent of the resultant gases liberated consisting of this lethal substance in question. As the composition of gunpowder is variable, the quantity of gases evolved and their relative proportions vary with the type of powder that has been used. For instance, the so-called cocoa powder contains 79 per cent of nitrate of potash, 2 per cent of sulphur, 18 per cent of charcoal and 1 per cent of moisture; black rifle powder contains 75 per cent KNO_3, 10 per cent sulphur and 15 per cent carbon, while blasting powder contains 67 per cent of nitre, 19 per cent of carbon and 14 per cent of sulphur. The volume of gases evolved during the explosion of these three explosive mixtures, when reduced to N.T.P., is as follows, in each case 1 kilogramme of the explosive being used: in the case of cocoa powder 200 litres, from the black rifle powder 275 litres, and in the case of blasting powder 360 litres. From certain French powders from 263 to 278 litres per kilogramme is evolved on explosion.

The detonative decomposition of gun-cotton, which may be considered

as typical of the various compound explosives of which it forms part, may be expressed by this formula :—

$$C_{12}H_{14}O_4\,(NO_3)_6 = 7CO_2 + 5CO + 4H_2 + 3H_2O + 3N_2.$$

It will be seen from the above that in this case the percentage composition of the gaseous products of decomposition will stand for CO at about $22\frac{3}{4}$ while the gases are hot and the water present is in the form of fully vapourized steam, and about $26\frac{1}{3}$, or well over one quarter of the whole, when the water vapour has condensed out. In this latter case, no less than 859 litres of gas containing this high proportion of carbon monoxide, are produced—measuring at N.T.P. of course—from one kilogramme of the explosive. It is said that where, in certain special circumstances, a charge of gun-cotton burns instead of exploding, as much as forty per cent of carbon monoxide may be present in the fumes evolved.

It is the carbon monoxide thus produced, and produced in these high proportions and enormous quantities,[1] which is absorbed into the chalk and forced into the fissures, either existing naturally or resulting from the explosion of the charges that have been laid, that is being constantly encountered by those engaged in the work of the various tunnelling companies, and which frequently results in the occurrence of cases of gas poisoning of this specialized nature. Owing to the gas being contained in cracks among the chalk, it is found in what are described by the miners as "pockets," and owing to this fact in many instances the gas is liberated too suddenly for the men to notice any alteration in the behaviour of the test animals (mice or canaries) that they have with them before they are themselves beginning to be affected. Usually the amount of gas set free by the disturbance of one of these "pockets" is not too great to prevent a realization of their symptoms, in which case they usually seek the fresh air at once.

An official document affirms that "the formation of large quantities of combustible gases—CO, H and CH_4—is generally indicative of poor detonation." Their presence depends, however, on the essential nature of the explosive used, though in a certain sense the occurrence of these gases in the galleries may depend on imperfect detonation. Where a well-detonated charge has been expected to break the surface a vent will of course be formed, permitting escape into the atmosphere of the gaseous products of the explosion. Where, on the other hand, the charge has failed to detonate properly (whether from an insufficient number or distribution of the detonators in a large charge, from deterioration of the explosive from damp or other cause, from imperfect tamping or the operation of other factors), the surface may not be broken, and the gases formed are forced under pressure into the surrounding broken-up ground from which they make their way sooner or later into neighbouring galleries, the

[1] For comparison it may be mentioned that the gases from a blast-furnace contain from 27 to 36 per cent of carbon monoxide.

leakage of gas into the workings sometimes continuing over a period of many days, and being aided, as has been noted already, by factors such as a falling barometer and a rise in the level of the subsoil water. In an impervious stratum, such as clay, which occurs largely along the northern sector of the Flanders front, the difficulties met with owing to the late presence of gas in the workings after a blow (as the explosion of a small mine or camouflet is often termed) are very slight compared with those occurring where the galleries run through chalk or other substances of a porous or permeable nature.

In the two examples here described, the gas must have existed in some such "pocket," but was liberated in such large quantity that the men working at the face were rendered comatose with great suddenness, and when an officer, Captain Hough, M.C., R.E., had his attention directed to the occurrence he heard, he tells me, the stertorous breathing of the unconscious men as he was coming along the gallery, and before he had actually come in sight of either of them.

Captain P. T. Hough's Report.

"X was originally an incline ninety feet long dipping one in three, at the end of which was a 60° shaft going to a total depth of forty-five feet. From this, inclines were drawn in the form of a V. On April 26, the enemy blew a large charge about 120 feet from the shaft.

"On June 1 the left branch was blown with a charge of 20,000 pounds of (explosive),[1] being then 110 feet from the shaft and about seventy-five feet from the surface. The shaft, although tamped, was so badly damaged as to make recovering it too long a process. Two inclines, one in one, were accordingly started from the old shaft head. Men frequently complained of gas, and two or three mice and canaries were lost.

. . . . Work was continued in the left branch; several men were gassed, one or two having to go to hospital, during the days following. Most of these men complained of feeling very sick and even vomiting before a headache developed. In most cases a sleep in the fresh air and rest put the men all right.

"On June 30 I went down to listen in the left branch. The facemen complained of having felt sick from effects of the gas. I listened in this branch for about ten minutes, and then went into the right branch, travelling about ninety feet. Five minutes later I was called for from the junction, and on going into the left face, I found the two facemen . . . unconscious, with every limb twitching violently and the breathing stertorous: I heard the breathing even before seeing the men. With some difficulty we got them to the junction whilst the stretcher was

[1] The enemy is known to use charges of from 4,000 to 15,000 kilogrammes; their explosives being donarite, westfalit, trinitroanisol and glukauf, as has been proved by taking them over along with a district.

being brought down. One of the two men was sick whilst being taken out into the trench and still unconscious.

"Those of us who had taken the men out of the mine were very exhausted and strongly inclined to vomit on reaching the fresh air. On reaching the trench oxygen was administered . . . until breathing became normal: the men were then carried down to the dressing station where the other man was sick, though still unconscious. It was noticeable that their faces were quite a deep pink in colour.

"The men were then taken to a well-ventilated dug-out and put in charge of stretcher-bearers. One of them woke up during the night to urinate, but the other slept on until well into the following afternoon. They were then . . . sent to hospital."

(Signed) P. T. HOUGH,
July 7, 1916. *Captain, Royal Engineers.*

The story given by the two men themselves, however, when seen three days after they had been gassed, is to the effect that while at the mine face together they began to feel dizzy and came out into the fresh air. After about half an hour, one of them still feeling dizzy, they returned to the working face and after working there for about twenty minutes became unconscious and had to be carried out. This occurred, so far as I can gather, about seven o'clock in the evening; the one says that he remained unconscious (or rather sleeping) till one o'clock the next afternoon, while the other maintains that he was unconscious for twenty hours. They both, three days after the gassing, complained of a feeling of debility with headache and slight pains across the front of the chest. Both were constipated; one had vomited as late as two days after having been gassed: in neither was there any elevation of temperature, one of the two having his temperature subnormal, the thermometer registering 97·2° F.

Thirteen days after the cases of gas poisoning recorded above there was a further series of cases occurring in the same situation. On July 13 the ventilating pump was stopped for a short time in order to enable listening to be carried out without interruption by extraneous sounds. Within a short time two officers and a private were gassed, none of the cases being serious however. Both the officers complained of headache, palpitation and temporary debility, but were soon all right, and were able to carry on with their duties. From the private a more detailed story was obtained.

He says that he was gassed at his place "in the face" while engaged in listening. He felt pains in the head, and ached all over, and so he came out into the fresh air. On coming out he fell and lay where he was for about five minutes; he then got up and walked for about thirty yards, when he felt so exhausted and had such palpitation that he had to sit down. The next time he got up he walked a little farther, perhaps fifty yards, before he had to sit down again and rest. Then he proceeded to where he got a drink of hot tea, which he vomited in about half an hour. The next morning he was aching all over and could not get up, so he spent the day

in his billet. The following day he felt weak, and had slight headache, with slight looseness of the bowels; his temperature was 97° F.

The following are two striking examples of the way in which the gas collects in cracks in the chalk, from which later on it works its way and causes symptoms among those working in the vicinity. The case in which the man was struck down at once by the gas issuing from a crack that he had uncovered is particularly interesting, as in these *foudroyant* cases of gas poisoning the test animals taken down into the galleries naturally fail to give preliminary warning of the presence of the gas, and for this reason their value as indicative of its presence has sometimes been discounted.

"M. L., aged 43, was gassed two days ago while taking out the tamping from a mine that had been blown four days previously. While removing the tamping he came on a crack on the floor of the gallery, 'and the gas just spewed out,' rendering him immediately unconscious—*foudroyé* to use Brouardel's description. He remembers nothing of what happened, being carried out comatose, and coming to during a two hours' rest in a dug-out. Was sent to hospital, returning from there yesterday. Is weak; sweats profusely, and has no appetite."

"J. K., aged 22, was engaged yesterday in driving a gallery through the chalk near an area that had been disturbed by the blowing of a camouflet a week before. There were two or three long cracks in the chalk, a quarter of an inch wide, and running obliquely and vertically along the entire length of the face, the result of the explosion. After working for two hours he began to have a slight headache, and at the end of the shift felt very feeble and had weakness of his legs. On coming into the open air he felt worse and sat down in the trench for a quarter of an hour before proceeding further. On getting to the dug-out he could not eat, but had a drink of tea. After lying down for six hours he felt no better, and was sent back to billets. This morning feels weak on the legs, has slight headache and complains of tightness in the chest. Is pale, and appetite is poor; otherwise his condition seems very fair. Temperature 98·4° F. The officer who sent this man out of the trenches believes that he is malingering."

Part II.

Carbon Monoxide Poisoning from the Use of Blasting Charges in Military Mining.

Carbon monoxide poisoning is caused by the use of blasting charges on the working face during the military operations carried out by tunnelling companies. While driving a tunnel, footage may be obtained in one of two ways: either by straightforward pick and shovel work, or by breaking up the material at the face by means of blasting charges placed in borings and suitably tamped in. The latter method is specially useful where a gallery is being driven through a hard stratum, and where working in chalk

it is found that this becomes progressively harder and more compact in the deeper levels.

As has been shown, a wide range of explosive substances, from old-fashioned gunpowder on the one hand, to the modern high explosive compounds on the other, generate carbon monoxide on detonation, owing to their containing insufficient endogenous oxygen to oxidize completely all their carbon atoms during the sudden regrouping of elements that occurs when the explosion takes place.

Not only is this toxic gas produced by the explosion of a mine, whether one of our own or one fired by the enemy, but carbon monoxide is present in the fumes given off by many of the blasting-charges at the working face of the mine gallery. An exception must be made in the case of dynamite where this has detonated properly, as theoretically this substance, owing to the high oxygen content of the nitroglycerin it contains, should completely oxidize all the carbon present into CO_2, and have enough oxygen left over either to be liberated as such, or to form by combination with the nitrogen present a certain quantity of the higher oxides of nitrogen; which latter, although highly toxic, are to a certain extent brought down by moisture and are at once fixed and rendered innocuous in contact with any of the carbonates of the alkaline earths, such as are abundantly present where work is being carried out in the chalk. With blastine, geglinite, and cheddite, all of which are used in working on the face, it would appear that a certain amount of carbon monoxide is formed which in a small gallery may, even in the presence of good ventilation, give rise in susceptible persons to minor symptoms of poisoning, sufficient, perhaps, to interfere with their working for a longer or shorter period. Although cheddite contains chlorate of potash in addition to its other constituents (nitrotoluene and a resinous body), its use at times gives rise to symptoms similar to those met with where other explosives have been employed, that are unquestionably the result of the presence of carbon monoxide in the fumes. Two sticks of cheddite, weighing together only 100 grammes, detonated on the working face, have been known to evolve sufficient carbon monoxide to affect a man engaged afterwards in clearing away the broken-down chalk that had been loosened by the explosion. There is no question, however, that some men are more easily affected by the toxic fumes than others—in the same way as some men more than others have a more or less unconscious tendency to exaggerate their symptoms.

The following examples are illustrations of the effect of such blasting charges in giving rise to "mine gas poisoning" from carbon monoxide:—

Case 1.—Sapper J. M., aged 33. "Two days ago was gassed with CO on going into mine gallery two hours after a blasting charge of one and a half cartridges of cheddite had been fired in a borehole. He went up to the face and did a little work among the broken chalk, when he became groggy at the knees and his head began to spin. The gallery was properly

ventilated at the time. He came out of the mine, but when he got to the bottom of the shaft he required to have assistance. On getting into fresh air he collapsed, and does not well remember what happened. In about an hour he was all right again except for headache, but rested for the remainder of the shift. Now feels week about the legs and has a very poor appetite; is drowsy and tired, and has slept more heavily at nights since being 'gassed.' Is constipated. Temperature 98° F."

This case is a somewhat remarkable one owing to the length of time that elapsed between the blasting of the charge and the man being gassed. The reason is probably that there was a quantity of the gas forced into and among the broken chalk, and that when he began to stir it up with his shovel enough carbon monoxide was disengaged to give rise to symptoms. He was probably stooping down over his work and would inhale the fumes directly into his lungs.

Case 2.—Sapper I. B., aged 24. "Two days ago was working at the face in the mine; ten minutes (or so he says) after two blasting charges of cheddite had been exploded to break up the material at the face. The smoke was 'working out very steady' as he worked. After half an hour at this work the shift finished and he came out. During this time his head had been spinning, but he had not felt badly any other way. On getting into the fresh air he fainted suddenly. On coming to he walked slowly down to the aid-post in the trenches, but when half way there had to stop for five or six minutes owing to a fresh accession of faintness. Now complains of pains in head; tongue and hands are tremulous; temperature 99° F. The following day his temperature was 98° F., and he was otherwise much about the same."

Case 3.—Sapper G. L., aged 24. "Has a septic mouth with diffuse toxic pains and headaches. Regardless of true etiology, he attributes his discomforts to 'eating the smoke' (*i.e.*, to use another of his phrases, 'swallowing a mouthful of the smoke') of the cheddite charges used for blasting in the mines, and says—in this case probably correctly—that he always gets headaches when he has to work where a charge of cheddite has been exploded recently."

Case 4.—Pte. F. S. (attached infantry-man), aged 22. "On the previous day was down a mine when a blasting charge was fired at the working face about fifty yards away. About a quarter of an hour afterwards he resumed his work of pushing a trolley loaded with bags of broken chalk from this face to the bottom of the shaft; while employed at this he became short of breath and began to feel weak; and when, ten minutes after he had restarted working, a charge was blown in another gallery, and white smoke from it began to come into the one where he was, he felt so weak that he came out of the mine of his own accord. While climbing the ladder in the shaft, he felt as though he might collapse and fall off at any moment, and, on reaching the open air, he had to lie down for ten minutes. At present he is very confused, and mixes up his story so that it is with the greatest

difficulty that any sense is got out of him—to get this story took over half an hour—and he says that he has taken no food since being gassed, not owing to any feeling of sickness but to complete loss of appetite. Tongue dry and denuded, bowels regular, temperature 98·2° F."

In mining operations in civil life, carbon monoxide poisoning is not unknown as the result of the use of blasting charges on a working face, but in these cases the quantity of explosive is very much greater than in the charges dealt with here. For instance, in the mines of Johannesburg a charge will consist of from 40 to 50 lb. of blasting gelatine distributed in fourteen or fifteen drill holes on the face and all detonated within a few seconds of one another by time fusé. The quantity of carbon monoxide evolved by the explosion of such a quantity of blasting gelatine may be considerable; but the quantity of deleterious gas generated from even a stick and a half or two sticks of explosive at the working face in one of the galleries in military mining is, as is pointed out here, quite sufficient to give rise to trouble.

The following are notes on the fumes of some explosives used in blasting on the working face in military mining operations, compiled for me by Lieutenant W. A. Ellison, Royal Engineers.

"*Blastine.*—This gives an exceptionally dense fume of a white colour and is very difficult to clear even with a strong current of air. It is impossible to breathe long in these fumes, which cause intense headache.

"*Dynamite.*—The bluish-white fumes from this are very heavy and remain low. With this explosive I find it is possible to breathe fairly well long before the gallery is clear. In this respect it is unlike "blastine." The effect of these fumes is to cause vomiting—but very little headache.

"*Gelignite.*—This explosive does not give a very dense fume, and it is possible to get into a face quite soon after an explosion without any ill-effects. It clears itself fairly quickly even without a current of air. The fumes are white in colour.

"*Cheddite.*—As regards fumes this explosive is the best. Many times after firing I have at once gone to the face and remained there without the slightest inconvenience. The yellowish fumes seem to clear themselves much quicker if gelignite has been used with the cheddite, but the fumes are much denser than when either explosive is used singly."

Clinical and other Notes.

CLINICAL RECORDS OF VACCINE THERAPY IN THE TREATMENT OF WOUNDS.

By Captain C. SAMUT.
Royal Army Medical Corps.
AND
Captain W. T. MUNRO.
Royal Army Medical Corps.

It seems to us that vaccines are not used to their full advantage in the treatment of wounds with prolonged suppurations. There are probably various causes for this indifference to the use of vaccines, and the most common cause is that failure to achieve success is not uncommon.

The chief causes of failure are :—

(1) An injudicious selection of cases. Obviously cases where there is bone which will eventually necrose will not have their discharge cease as a result of vaccine therapy ; likewise cases of synovitis where the circulation to the part is somewhat poor are not going to benefit as much as a case involving only the muscular planes.

(2) Insufficient drainage. The surgeon must do his part. Pent-up pus or insufficient drainage is always a bar to successful vaccine therapy.

(3) Faulty dosage ; an improper appreciation of the indications for repetition or increase of dose.

(4) The want of response of the organism to the vaccine.

The following cases may serve to illustrate the value of vaccine therapy in selected cases and where the dose and indications for increase have been carefully weighed.

Case 1.—Captain N., admitted to hospital December 15, 1916, wounded November 30, gunshot wound, left shoulder. His history shows that he had incisions made on the posterior surface of the arm on December 16, and was drained. X-ray showed comminuted fracture. Again on December 29 further incisions were made over the biceps and on the inner side of the vessels. Discharge was profuse and drainage was free.

We were called to see him on January 1. He had been running a very septic chart since December 15, evening temperature about 100° to 101° F., pulse 100 ; morning temperature 99° F. and pulse 90. He was a very pale young man, soft-looking, with poor resistance, and with little spirit in him. The wounds were very dirty, several incisions round the shoulder poured with pus, and a direct film showed streptococci. Drainage was very free and the arm was put up on a Thomas's straight splint and dressed twice daily.

A vaccine was made, strength 20 million streptococci per cubic centimetre. The present condition was as above indicated ; on January 3, evening temperature 101° F., pulse 90 ; it was decided to give him not more than 10 million ($\frac{1}{2}$ cubic centimetre) ; he had his first dose on January 4. By night his temperature had

risen to 102° F., pulse 110; on the same day pus was very profuse. 5th: No local reaction and not observable focal result; evening temperature 99° F., pulse 100. 6th: Evening temperature 101° F., pulse 90. 7th: As the temperature had shown a tendency to rise, he was given the same dose again (10 million); evening temperature 100° F., pulse 90, no appreciable negative phase. 8th: Evening temperature 99° F., pulse 88; no local reaction; focal reaction, less discharge; generally expresses himself as feeling better. 9th: Evening temperature 99° F., pulse 80. 10th: Evening temperature 99·4° F., pulse 102 (end of positive phase). 11th: Evening temperature 100° F., pulse 96. 12th: Tendency to rise again and another ½ cubic centimetre given; evening temperature 100·4° F., pulse 92, slight negative phase. 13th: Evening temperature 100·2° F., pulse 88, slight negative phase. 14th: Evening temperature 99° F., pulse 92, positive phase. 15th: Evening temperature 99° F., pulse 80, positive phase; focal reaction, much improved, much less discharge, wounds healing. 16th: As the tolerance to the 10 million dose was clearly established, with a view to obtaining a better positive phase he was given 20 million (one cubic centimetre). 17th: Evening temperature 100° F., pulse 94. 18th: Evening temperature 98·6° F., pulse 76, positive phase. 19th: Evening temperature 97° F., pulse 66, positive phase. 20th: Evening temperature 98° F., pulse 64, positive phase. 21st: Evening temperature 99° F., pulse 72, positive phase; general condition much improved; temperature and pulse steady; looks much better, much cheerier in disposition, takes his food well; wounds healed except for two small sinuses. 22nd: Evening temperature 98° F., pulse 68. 23rd: Evening temperature 97° F., pulse 86. 24th: Given one cubic centimetre (20 million) one week from last dose; evening temperature 98° F., pulse 64. 25th: Evening temperature 98·6° F., pulse 72. 26th: Evening temperature 98° F., pulse 80. 27th: Evening temperature 98° F., pulse 72. February 4: Quite healed, bone shows union, and no evidence of necrosis.

Summary.—This man represents a case where the conditions were favourable from the onset. He was much reduced by his septic discharge, and had reached a state where his general resistance was very poor as evidenced by his pallor, lethargic condition and frequent formation of fresh foci of suppuration. He was freely drained from the onset, and bone did not seem to be septic, but sepsis was confined to the muscular planes. Such a case was one whose resistance could reasonably be stimulated by an autogenous vaccine.

Case 2.—Lance-Cpl. P., 1/South Staffs. Wounded October 4. Shrapnel wounds left thigh, also wounds below the knee. Admitted to Fort Pitt November 21. Leg very septic, muscles soft and breaking down easily. Leg not swollen, destruction of tissue very marked and progressive. Pressure on the thigh causes pus to well out at all the openings, and the femoral artery was exposed in places. On November 22 the openings were enlarged and the wounds packed with "Bipp." We were called to see him on the 22nd. The surgeon wished something tried, as he feared erosion of the artery consequent on the great destruction of tissues. This had been an unfortunate occurrence in previous cases. When called to see him he looked very ill, with pale and pinched expression. Morning temperature 97° F., pulse 138; evening temperature 102° F., pulse 140; tongue dry and leg as above described. The wounds on the leg (not the thigh) were somewhat less purulent. Streptococci on direct film; vaccine made, 20 million per cubic centimetre. On the 24th a small dose

was given, 10 million, as his general condition was poor. Evening temperature 101·2° F., pulse 138. 25th: Evening temperature 100·2° F., pulse 118, positive phase. 26th: 100·2° F., pulse 118, positive phase. 27th: Evening temperature 101·2° F., pulse 128, positive phase; no focal result. 28th: Tendency to rise and another 10 million given; evening temperature 100·6° F., pulse 128. 29th: Evening temperature 100° F., pulse 118. 30th: Evening temperature 100·6°, pulse 128. The positive phase was very poor, and it was decided to try a larger dose; there was still copious discharge, but there was also pus retained, preventing good reaction—one cubic centimetre (20 million) given to judge the effect. December 1: Evening temperature 100·6° F., pulse 130. 2nd: Evening temperature 101° F., pulse 128. 3rd: There seems to be no change with a larger dose. No local reaction and no focal reaction; evening temperature 100·8° F., pulse 118. 4th: Evening temperature 101° F., pulse 120. 5th: Evening temperature 101° F., pulse 124. The wounds below are much more healthy and no discharge from them, still pulse and temperature have not been affected by the last injection. On careful examination a pocket of pus is found on the posterior aspect of the thigh and this wants draining. 6th: Incisions on posterior aspect allowing excellent drainage. "Bipp" was cleared out of all the spaces, and it was decided to leave him in a bath one hour every day. With free drainage he began to improve; temperature falling, pulse slowing every day till the 12th, when it began to rise. Evening temperature 100·2° F., pulse 112. Given one cubic centimetre vaccine on the 13th. Evening temperature 101° F., pulse 120. 14th: Evening temperature 99° F., pulse 94, positive phase. 15th: Evening temperature 98° F., pulse 96, positive phase. 16th: Evening temperature 98·2° F., pulse 96, positive phase. 17th: Evening temperature 99·2° F., pulse 102; feeling better, sleeping better. 18th: Focal condition had much improved, much less discharge; and here he was given another one cubic centimetre, as he had shown a rise. Evening temperature 99·8° F., pulse 106, slight negative phase. 19th: Evening temperature 98·4° F., pulse 100. 20th: Evening temperature 97·8° F., pulse 94. 21st: Evening temperature 98·8° F., pulse 96. 22nd: Evening temperature 96·6° F., pulse 88. 23rd: Evening temperature 97·6° F., pulse 92. 24th: Evening temperature 96·8° F., pulse 88. 25th: Evening temperature 98° F., pulse 82. 26th: Given one cubic centimetre after one week. Wounds closing up; feeling absolutely well, eating and sleeping much better—discharge has now almost ceased. 26th: Evening temperature 98° F., pulse 100. 27th: Evening temperature 97° F., pulse 96. 28th: Evening temperature 97° F., pulse 96. 29th: Evening temperature 98° F., pulse 78. There was nothing further to report. He healed up entirely, was able to move the knee, and was discharged to a Voluntary Aid Detachment Hospital on January 2, 1918.

This case is interesting: (1) Because a very similar case had been in the same ward only a few days before and died of secondary hæmorrhage from erosion of the artery; (2) because whilst the results of the first two injections were promising, the third injection had very little, if any, effect on the patient, and the surgeon began to lose faith in the vaccine treatment. But a careful examination showed a pocket of pus on the posterior aspect of the thigh which accounted for the failure. This was opened and a large quantity of pus evacuated. When free drainage was established the patient made uninterrupted progress.

Case 3.—Pte. C., aged 22, Royal Fusiliers.

History: Slight wound of a finger in France which quickly became a whitlow. This was opened and he was sent to England and admitted to Chatham November 20, 1916. A large abscess appeared in the gluteal region about the 24th. This was opened and much pus evacuated. Temperature 101° F., pulse 120. Pus showed streptococci and a vaccine was made, 20 million per cubic centimetre. When seen by us on the 25th he looked ill. Temperature 101° F., pulse 124; face flushed, headache, and a large abscess cavity was present over the right gluteal region, and pus was very copious. On the 29th, had his first dose 0·5 cubic centimetre (10 million). There was no appreciable change, and on December 1, he was given a second dose of 0·5 cubic centimetre. The evening temperature fell from 101° to 99·4° F., and the pulse from 110 to 88. On the 4th, temperature was 99·2° F., pulse 92, and on the 5th, temperature rose again to 100° F., and pulse to 98, and it was found that another abscess was forming in the right scapular region. This was opened and pus evacuated. On the 6th, 0·75 cubic centimetre given and on that evening temperature went up one degree, but next day it came down to 100° F. and on the 8th to 98·4° F., and pulse 96. December 10, 1917: Temperature 101·4° F., pulse 98. A fourth injection 0 75 cubic centimetre given. A slight rise of temperature followed, but on the 12th the temperature was 100·2° F., pulse 100. 13th: 98·4° F., pulse 88. On the 16th, temperature 99° F., pulse 100, and on the 17th a fifth injection of 0·75 cubic centimetre was given. The temperature rose one degree, but on the 19th it was normal, and remained normal till patient was discharged on January 2, 1918.

Summary.—The abscesses that followed the septic finger at very short intervals suggested the possibility of a pyæmic process, and the surgeon in charge of the case feels confident that the vaccine therapy prevented the formation of fresh foci of suppuration.

Case 4.—Pte. M., Argyll and Sutherland Highlanders.

History.—Wounded April 23, 1917, gunshot wound right foot. This took a long time to heal, but eventually he was sent to a Voluntary Aid Detachment Hospital. He was readmitted November 17, 1917, with pus in the right knee-joint. This was aspirated and the joint injected with formalin, iodoform and glycerine. Later it was found necessary to make small openings into the joint. The acute arthritic condition died down considerably, the joint was not swollen, but discharge continued, and patient ran a septic temperature varying from 101° to 103° F. in the evening and 99° F. in the morning. December 26, 1917: When seen by us he was very thin, worn and with a hectic flush on the face; not taking food well, and sleeping badly. There were small openings around the knee-joint discharging a fair amount of pus. The knee-joint was not swollen and was fixed in a semi-flexed position. The synovial membrane was not affected, but the tissues around the joint were infiltrated and discharging, but not freely. There were also purulent openings in the leg, and there was a discharge from a wound in the foot. Pus shows streptococci. Vaccine made, 20 million per cubic centimetre. On 29th, although drainage was not free, and under the circumstances we do not expect any great result from a vaccine, still we gave him three injections of 0·5 cubic centimetre at intervals of about six days, depending on the rise of temperature. With each injection there was a slight negative phase, but the positive was of very short duration and no real improvement followed. Then

it was decided on January 16, 1918, to open up all the tracks of the purulent process. 17th: Given one cubic centimetre (20 million); temperature 100·4° F., pulse 116. 18th: Temperature 100° F., pulse 110. 19th: Tempera- 102·4° F., pulse 128. There was no improvement with this dose, but a collection of pus was forming on the outer side of the thigh. On the 20th this was opened and pus evacuated. 21st: Evening temperature 100·2° F., pulse 116. 22nd: Given 0·5 cubic centimetre (10 million); temperature 101° F., pulse 110 (negative phase). 23rd: Evening temperature 98·4° F., pulse 84. 24th: Evening temperature 98·8° F., pulse 90. 25th: Small dose seemed to suit him very well, and as his temperature had risen slightly he was given 0·5 cubic centimetre again; there was no negative phase; evening temperature 97·8° F., pulse 88. 26th: Evening temperature 98·2° F., pulse 76. Much less discharge now. Wounds healing; knee has been straightened and fixed in much better position. Patient expresses himself as feeling much better. 27th: Evening temperature 98·4° F., pulse 80. 28th: Evening temperature 98° F., pulse 80. 29th: Evening temperature 98·2° F., pulse 92. 30th: Evening temperature 99° F., pulse 100. 31st: Given 0·5 cubic centimetre. February 4: Temperature and pulse have remained subnormal. Discharge has now ceased.

Summary.—The case is interesting because it shows that as long as there is pent-up pus vaccine therapy is of little avail.

Case 5.—Pte. I., 1/4th King's Own Yorkshire Light Infantry.

History.—Wounded October 9, 1917, left thigh by a splinter from a bomb during an air-raid, admitted Chatham October 19. Wound ulcerated, ulcer excised on October 24, but the edges broke down, and the destructive process continued. When seen by us on December 2, ulcer size four inches in diameter with sloughy edges and membranous exudation covering the surface. Direct film from the sloughs showed staphylococci and diphtheroids. Vaccine made, 1,000 million staphylococci per cubic centimetre. On the 5th was given 500 million. Evening temperature 99° F., pulse 90. No local reaction. 6th: Evening temperature 98° F., pulse 80. 7th: The membranous exudate easily removed with forceps. Ulcer looking much better. Evening temperature 97·8° F., pulse 80. 8th: No change in focal condition. Evening temperature 98° F., pulse 100. 9th: Given another 500 million as the pulse had risen. Evening temperature 99° F. pulse 102. 10th: Evening temperature 98° F., pulse 80. 11th: Evening temperature 97·8° F., pulse 82. Ulcer shows healing edge and clean healthy granulations. There was nothing special to note during the next few days, as the improvement was maintained. On 16th he was given 1,000 million with a view to keeping his resistance good. He had little reaction. Temperature 99° F., pulse 100. The ulcer healed in the usual way. There was a large surface to granulate, but progress was uninterrupted, and he was discharged healed on January 2, 1918.

Summary.—The surgeon in charge is emphatic that there was no progress until vaccine therapy was commenced, in fact the infection caused the edges to break down and the ulcer to increase.

These cases are representative of wound infections where with suitable selection and favourable conditions, vaccines proved of great service.

A GERMAN BULLET EMBOLUS.

By Captain H. J. B. FRY.

Royal Army Medical Corps (T.F.).
Pathologist to No. — General Hospital, British Expeditionary Force, France.

This case is recorded as a remarkable instance of the migration of a rifle bullet in the venous blood-stream. Previous cases have been noted of the movement of foreign bodies in the vascular system.

In this instance there was a small oval wound of entry ½ inch below the left anterior superior iliac spine. It will be seen below that the bullet entered the vascular system by penetrating the left external iliac artery, causing an arterio-venous aneurysm of this artery with the left internal iliac vein. From this

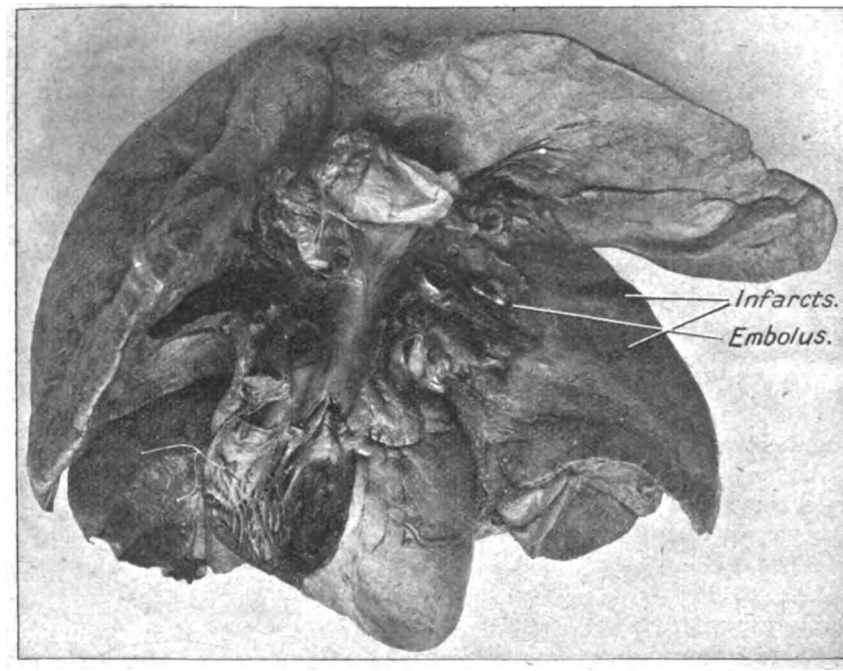


Fig. 1.

position the bullet was carried up the common iliac vein and the inferior vena cava. It passed through the chambers of the right side of the heart, through the pulmonary valve into the left branch of the pulmonary artery where it impacted as an embolus in one of the branches supplying the lower lobe of the left lung, thereby causing two infarcts in this lobe (*vide* fig. 1).

Such a tortuous and deflected course is in itself remarkable, but in addition there was no injury to be found either of the veins which it traversed or of the flaps of the tricuspid and pulmonary valves through which it passed. It is astonishing, on consideration, that the bullet should not have been entangled

in the meshes of the chordæ tendineæ and musculi papillares of the right ventricle. Moreover there was never any pain or discomfort referred to the heart or the lungs.

The question naturally arises whether this bullet could have found its billet by any other path. The clinical evidence and post-mortem findings prove without question that the bullet could only have reached its final situation by the above route, as there was no other wound of the body and no other place of entry into the vascular system except the above mentioned aneurysm.

The history and course of the case present some interesting features in addition to the post-mortem findings. The notes of these are therefore added.

Clinical Abstract.—Patient stated that he was standing by his battery position on April 2, 1918, when he suddenly felt a sharp stinging pain in the left foot, and thought that he had been hit there by some missile. His boot was taken off but no wound could be found. He was unable to walk and was carried to the field ambulance, where his leg was examined and found to be swollen and congested. A small wound below the left anterior superior iliac spine was found, but nowhere any wound of the leg. On admission a small oval suppurating wound apparently superficial, was found immediately below the left anterior superior iliac spine. There was no evidence of penetration and no track could be found. The left foot was puffy and discoloured, and there was no capillary reaction. No pulse could be felt at any point in the leg. A wide-spread ecchymosis beneath the skin of the left loin and left iliac fossa and a well marked humming murmur heard at its loudest about 2½ inches below and to the left of the umbilicus together with a thrill, afforded a diagnosis of an aneurysm of the left external iliac artery.

The whole of the left leg was considerably swollen and œdematous. The patient continually complained of much pain in this leg. The temperature was normal on admission but the pulse was rapid (100-120), full, but of low force and tension. The pulse rate was rapid throughout the course of the illness.

X-ray report was, "no evidence of foreign body from level of umbilicus to knees."

For a week the patient's general condition remained good. There was some collapse of the bases of both lungs. A hæmic systolic murmur was present at the apex of the heart, and it was especially loud in the pulmonary area. The pulse was rapid (136 per minute), full and soft. Blood-pressure 95 to 100 millimetre Hg., respiration was rapid 36 per minute and shallow. There was a slight icteric tinge of the skin of the face and conjunctivæ and considerable œdema of the back. Urine showed a faint trace of albumin, a few renal epithelial cells, and and one or two degenerated granular casts. Ten days after its receipt, the wound was almost healed and the ecchymosis of the loin had disappeared but gangrene of the leg was complete and the leg was therefore amputated below the knee by Captain le Mesurier, R.A.M.C.

The patient's condition improved for a short time, but in a few days the amputation stump became gangrenous. A booming cavernous note was detected in the aneurysmal murmur as though the aneurysm had enlarged, and the respiration, which had always been shallow and rapid, became gasping and very rapid, with a greatly increased pulse rate. Finally the patient became delirious, the pulse rate was uncountable, and the respiration rate rose to 60 to 70 per

minute. The temperature steadily increased and the patient gradually sank and died in coma.

Post-mortem Notes.—(1) Bullet wound left groin; (2) arterio-venous aneurysm of left external iliac artery and left internal iliac vein; (3) gangrene of left leg.

Peritoneal cavity was free from adhesions or fluid except for a small quantity of blood-stained exudate. The whole of the sub-peritoneal tissue planes in the region of the left iliac fossa and left psoas muscle were ecchymotic, the ecchymosis extending into the pelvis and across to the right iliac fossa.

There was a large fluctuating swelling commencing at the lower part of the common iliac artery and vein. Its periphery was ill-defined. The abdominal aorta was found collapsed and rather shrunken and the left common iliac artery

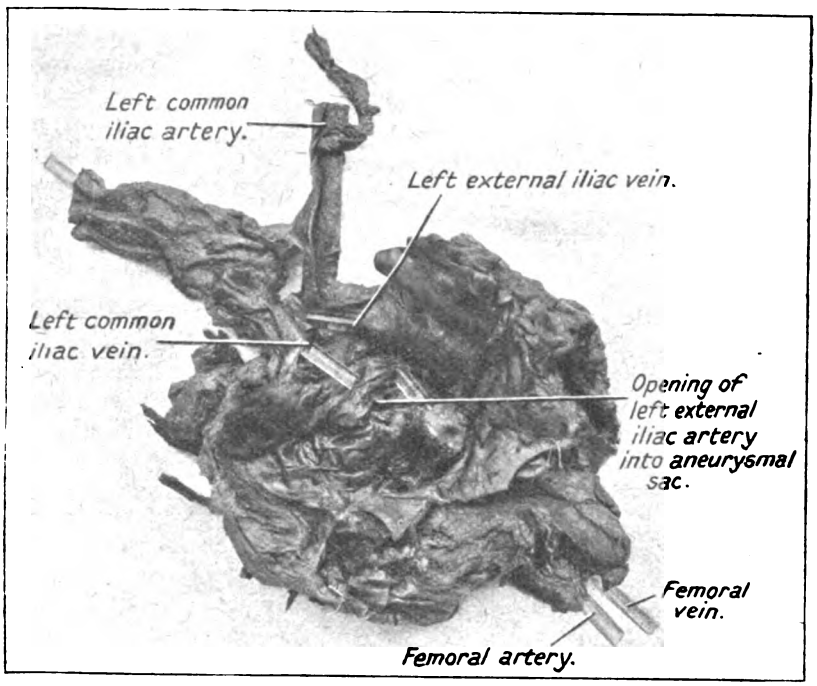


FIG. 2.

was small. Both vessels contained a little recent clot. The inferior vena cava was large and dilated and full of dark fluid blood. The renal veins were large and both common iliac veins were distended, especially the left. The left femoral artery was small, collapsed and empty, but the femoral vein and internal saphenous vein were large and thrombosed.

The aneurysm was ligatured above at the common iliac artery and vein and below at the femoral artery and vein. On dissection it was found that the left external iliac artery had been penetrated along its posterior aspect, immediately below the origin of the left internal iliac artery. The externel iliac artery entered, by a bevelled opening, the anterior wall of a large saccular aneurysm about four

inches long by 3½ inches wide formed by the internal iliac vein. The external iliac vein lay in the anterior wall of the aneurysm with a crescentic opening into the apex of the sac. It was completely thrombosed below this opening. The external iliac artery was patent both above and below its opening into the sac (*vide* fig. 2).

The abdominal organs showed a condition of chronic passive venous congestion.

Liver was enlarged, hard in parts and showed a typical "nutmeg" appearance.

Spleen was slightly enlarged, dark coloured, tough and elastic. Kidneys showed congestion at base of the pyramids, but were free from marked changes.

Pleural cavities contained a small quantity of blood-stained exudate. There were no adhesions except at the apex of the left lung.

Pericardial cavity contained a slight excess of clear fluid. There was no pericarditis or adhesions.

Right lung showed a moderate degree of collapse at the base of the lower lobe and posterior border. There was a slight compensatory emphysema of the upper lobes.

Left lung showed an infarct four inches from base of the lower lobe immediately below the inter-lobar fissure extending to the anterior border of the lung. The infarct was dark red, very hard and well defined, size 4½ inches by 1½ inches broad. The adjoining lung tissue was healthy.

There was a smaller infarct 1¼ inches above the larger infarct near the anterior border of the lower lobe.

The lower lobe showed a moderate degree of collapse of the base and posterior border. There were a few small areas of collapse in upper lobe.

Heart was opened in situ while attached to the lungs in order to determine the cause of the infarcts. Veins of the chest and neck were engorged with blood.

The right ventricle when opened was slightly dilated. It contained a quantity of dark fluid blood. The tricuspid valve was normal in appearance.

The pulmonary valve was intact and healthy. The cusps were normal. The right branch of the pulmonary artery was healthy and contained fluid blood. The left branch of the pulmonary artery presented no abnormalities, but on opening the branch running to the lower lobe of the left lung the scissors points grated on a metallic body. This was found to be the base of a rifle bullet which was very firmly wedged in the lumen of the vessel surrounded by a small quantity of fibrinous clot. The bullet was in perfect shape with its axis directed in the course of the vessel, and its apex wedged firmly into the vessel completely occluding its lumen and by its lateral aspect blocking the opening of a smaller branch, thus causing the second infarct.

Appendix.

Weights of abdominal organs :—		
Liver	65	oz.
Spleen	10	,,
Right kidney	4½	,,
Left kidney	6	,,
Weight of bullet	10	grms.
Length	2·8	cm.
Circumference	2·2	,,
Diameter of base	0·7	,,

Discussion.—From measurement in situ and standard measurements the distance travelled by the bullet in the blood-stream was not less than two feet (about sixty-five centimetres). Since the blood-pressure in the inferior vena cava in the normal condition stands at about three millimetres Hg and increases in the veins of the chest and right auricle to eight millimetres Hg, while the velocity of the blood is not more than twenty-five cubic millimetres per second, it is evident that the blood-pressure in the abdominal veins must have been greatly increased through the formation of the arterio-venous aneurysm, to have enabled the venous flow to sweep such a comparatively heavy weight as ten grammes along the veins. Raising of the venous blood-pressure no doubt accounts for the continuously rapid pulse rate, which never fell below 120 per minute, and for the rapid rate of respiration, 30 to 40 per minute, rising in the later stages to 60 per minute. The condition in fact was one in which the patient was bleeding into his venous circulation. This is supported by the comparatively low arterial blood-pressure, 95 to 100 millimetres Hg, and the full, soft collapsing pulse. The raised venous blood-pressure is evidently the cause of the dilatation of the veins, and the rapid establishment of the condition of chronic passive venous congestion of the abdominal organs, which was found post-mortem.

Freedom of the blood-stream from general infection and absence of suppuration at the site of impaction of the bullet were doubtless due to its uninjured and smooth surface.

The absence of any pain at the site of the wound, the intense pain referred to the foot and leg, both at the time of receiving the wound and subsequently, combined with the complete absence of pain in the heart or lungs, are interesting features. Some anginal pain might have been expected during the passage of the bullet through the heart, though the diameters of the pulmonary and triscuspid orifices are sufficient for the transmission of the bullet even in its long axis. As shown by X-ray the bullet had probably taken up its final position before admission of the patient to this hospital. Probably the smooth surface of the bullet and its "streamline" shape helped to lodge it so aptly in the pulmonary artery.

Summary.—The points of interest in this case may be summarized as follows:—

(1) The distance and deflected course travelled by a rifle bullet in the blood-stream.

(2) The formation of two infarcts in the lower lobe of the left lung by the bullet acting as an embolus.

(3) The absence of pain referred to the heart or lungs, the freedom from any syncopal attacks, and the absence of any infection of the blood-stream.

(4) The condition of marked, passive venous congestion established in the short period of a month.

The specimen has been forwarded to the War Museum at the Royal College of Surgeons.

I am indebted to Lieutenant Colonel Butler, D.S.O., for permission to use the notes of this case, to Colonel Pasteur, C.M.G., and Lieutenant-Colonel Martin, F.R.S., for their assistance and advice, and to Captain Fergusson, R.A.M.C., for the photographs accompanying the text.

NOTES ON A CASE OF BLACKWATER FEVER, TREATED BY PANCREATIC AMYLOPSIN AND TRYPSIN.

By Lieutenant-Colonel J. H. DOUGLASS.
Royal Army Medical Corps.
AND
Captain H. CARLTON.
Royal Army Medical Corps (S.R.).

The patient, Gunner E——, R.G.A., aged 25, with fifteen months' service, was admitted to the Military Hospital, Tower Hill, Freetown, Sierra Leone, on November 3, 1915.

A man of fair physical development and constitution, he had served in this station for seven months, and had had several attacks of subtertian malignant malaria, treated with quinine.

He had only been discharged from hospital a fortnight and was still on quinine treatment.

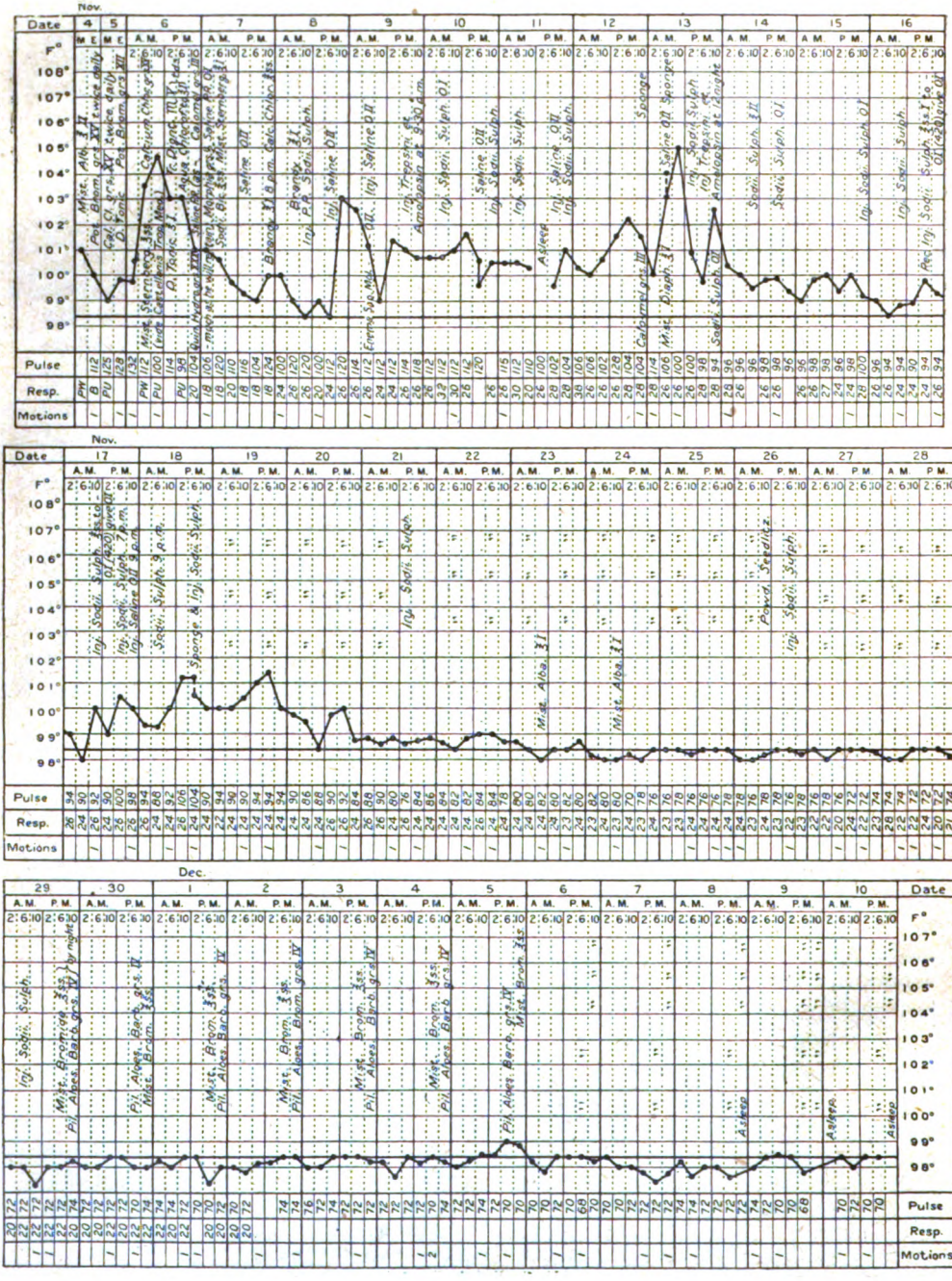
Condition on Admission.—Tongue furred, nausea, inability to retain food, headache, pains in loins, temperature 101° F., pulse 112. During the first few days his condition became rapidly worse; temperature 104·8° F., pulse weak, collapse very marked. Quinine could not be retained when given by the mouth, and three doses of eight grains were given "intramuscular." No malarial parasites were detected in the blood, but there was an increase of large mononuclears.

Treatment was directed to his collapse—brandy being given by the month and saline per rectum. A mixture containing tinct. digitalis was given, and also Sternberg's mixture (sodii bicarb. 150 gr., hydrarg. perchlor. $\frac{1}{8}$ gr., aqua ad 60 oz.) was given in large quantities, and retained. Billet's mixture (cal. chlor. 5 grm., sod. chlor. 10 grm., aqua dest. 1,000 grm.) was also given.

His temperature fell to 100° F. on the fourth day and remained down until the evening of the fifth day, when it rose to 103° F. and collapse was again extreme. The patient was delirious, very jaundiced, with melæna and hæmatemesis. The urine contained hæmoglobin and had acquired a dark porter tint.

It was at this stage that I decided to try the effect of injecting trypsin and amylopsin, which I had seen mentioned by one of our officers in Burma. I had ordered some from Burroughs Wellcome and Co., which however had not arrived, but Dr. Rice, the colonial Principal Medical Officer, kindly gave me some to try in the meantime. On the evening of the sixth day one ampoule of the trypsin and one of the amylopsin (Fairchilds and Co.) was injected into the substance of the glutei. Local reaction was slight, although we did not dilute the injection with normal saline as recommended.

The temperature during the seventh and eighth days and also the ninth remained at about 101° although on the ninth day the pulse rate fell from 115, which it had been for some days, to about 100. On about the tenth day the patient again became much worse, the temperature rose to 105·4° F. and he vomited; urine again contained hæmoglobin. A second dose of trypsin and amylopsin was given, and by 10 a.m. on the next day the temperature had fallen to 99° F., pulse 98. Two days later hæmoglobin had disappeared from vomit



and excretions. On the fifteenth and sixteenth days of his illness there was a slight rise of temperature and pulse-rate but this rapidly passed and an otherwise uneventful convalescence terminated the cure. On the thirty-seventh day of his illness he was invalided to England.

The attention of those who would say that *post hoc* is not always *proptor hoc*, is called to the clearness of the diagnosis from yellow fever on the one hand and from quinine hæmoglobinuria on the other.

Treatment, apart from the administration of trypsin and amylopsin, was directed entirely towards combating collapse, and keeping open the usual channels of excretion. In my opinion the case would have died only for the trypsin and amylopsin treatment. We have tried the same treatment on cases of subtertian malignant malaria with good results in many cases, although in some old cases parasites appear again in the circulation and quinine has to be resorted to. In first attacks amylopsin appears to sterilize the body of parasites, probably the asexual parasites are destroyed while the sexual forms escape. The injection has a decidedly stimulating effect; in one case I found the patient walking about the ward next morning although he had a temperature of 103° F. the night before when the injection was given.

At present the number of cases is too small to give a decided opinion, but the treatment appears useful in all malaria cases, especially first attacks in which sexual forms have not appeared. It is also a standby in cerebral malaria, blackwater fever and may perhaps be beneficial in yellow fever.

Clinical charts of case are given.

SEVEN-DAY FEVER IN ADEN.

By Captain W. F. M. LOUGHNAN, M.C.
Royal Army Medical Corps.

This fever has been so well differentiated by Rogers as to deserve a place in the official nomenclature of diseases.

At present in the official statistics it is returned under the obscure disease, "Pyrexia of Uncertain Origin," which conveys little knowledge as to the clinical or other nature of the fever.

The disease as it occurred on the Aden littoral, from clinical observation, leaves little doubt as to its being a very definite and separate fever, requiring classification. In British Arabia it is endemic, and attacks Europeans and Orientals with equal severity. The former are generally affected during their first two years of residence abroad.

Patients suffer from the disease irrespective of age. Males are more affected than females, relapses have not been seen, and in one case the fever was observed for two consecutive years.

General Condition and Appearance at the Onset.—The onset is generally sudden, the patient complaining of a feeling of chilliness, associated with a rigor and dull pains in the back. The face and neck are flushed and the conjunctivæ injected. The development of the fever is sometimes insidious, simulating

enterica, more particularly the paratyphoid A group, and enteric fever occurring in persons who have been artificially immunized by vaccination against enteric fever.

Digestive System.—The appetite is completely lost, but the patient does not suffer from excessive thirst. The tongue is coated centrally, the tip and margins are clean; a slight sore throat is occasionally present. At the onset of the fever the patient may vomit, but this is a rare occurrence; the abdomen is somewhat distended, the liver slightly tender, and the spleen is occasionally felt. Diarrhœa or constipation may be present, but the tendency is to have the bowels confined.

Circulatory System.—The heart shows nothing to note, the pulse-rate is in co-relation with the temperature for the first twenty-four or forty-eight hours, and is often full and bounding, after which the rate is diminished. Bradycardia is present at the end of the fever and during the early days of convalescence.

Respiratory System.—The respiratory system does not appear to be affected in this disease; a mild double basal bronchitis is sometimes present, and respiration is slightly increased during the first forty-eight hours of this fever.

Clinical Examination of the Blood.—The examination of the blood as a method of diagnosis shows nothing pathognomomic of the fever. From a careful study of the blood of twenty-five cases of undoubted seven-day fever, the following results were obtained: It was found that in eight cases the blood content was normal; in nine cases the total number of red and white corpuscles was slightly reduced. In the remaining eight a differential count showed the polymorphonuclear cells reduced, while the larger mononuclears (and to a lesser extent the small mononuclear cells) were relatively increased; of these eight cases three had a previous history of fever, which may have been malaria, and would help to explain the large mononuclear increase.

The Skin.—In a clinical examination of fifty cases the skin was smooth and sweating, rashes were noticed on two cases, the eruptions appearing all at once on the fourth and fifth days respectively. In both cases the eruption resembled a mild typical morbilliform rash, which disappeared before the temperature was normal, and was unassociated with itching or desquamation.

Nervous System.—Patients suffering from "seven-day fever" invariably have a severe frontal headache, and frequently complain of dull pains in the back. In the enteric-like cases, the intellectual functions are somewhat dull, the cranial nerve functions normal. Delirium was present in one case.

Urinary System.—Examination of the urine shows nothing to note, a trace of albumin is occasionally present.

Temperature.—The duration of the temperature in this febricula varies considerably. In the majority of cases the fever lasts from six to eight days, but may be slightly more or less. The fever may be continuous or remittent, and is occasionally intermittent in type.

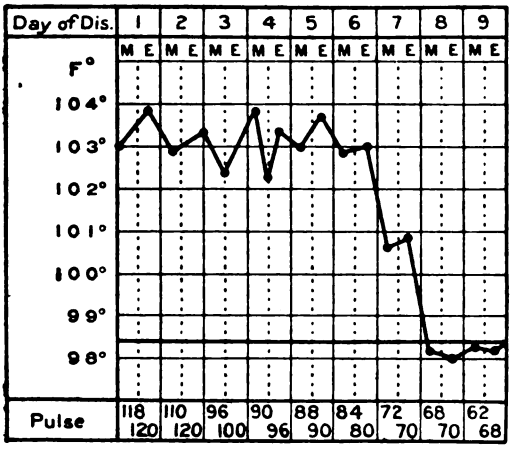
The temperature charts in this fever vary considerably; two varieties are commonly met with: one in which there is a continual daily fall in the temperature from the day the fever reaches its maximum until it becomes normal.

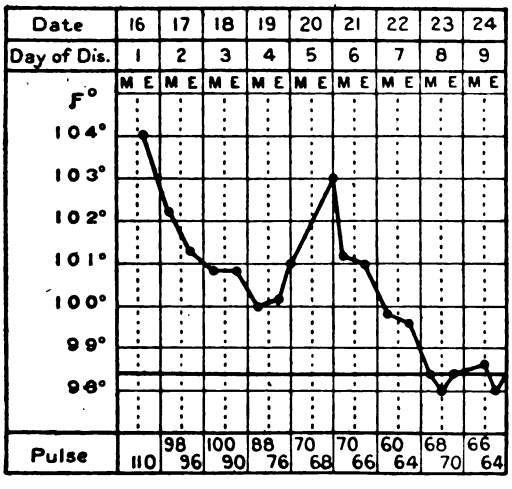
A second variety in which the so-called saddle-back temperature is seen, and where the temperature rises suddenly from 100° F. on the fifth day, to 103° F. on the sixth day, followed by a fall to normal on the evening of the seventh day.

Diagnosis.—Seven-day fever has to be differentiated from malaria, dengue, enterica, relapsing fever, sandfly fever, and influenza.

In the annual returns, the following is the number of admissions for "Pyrexia of Uncertain Origin" amongst the British Troops at Aden for the years 1908-1912:—

Year.		Cases.
1908	"Pyrexia of Uncertain Origin"	215
1909	" " " "	153
1910	" " " "	92
1911	" " "	36
1912	" " " "	29





In 1908, 215 cases of "Pyrexia of Uncertain Origin," 2 cases of enteric fever and 72 cases of malaria were recorded.

The monthly incidence of "Pyrexia of Uncertain Origin" was as follows:—

Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
1	0	3	8	11	68	64	28	12	12	8	0

The following table shows the number of days the temperature was above normal in the different cases :—

Number of days fever	1 to 4	5 to 7	8 to 10	10 and over
Number of cases	143	54	11	7

From the examination of the temperature charts of these patients, it was found that the fevers were either phlebotomus fever or seven-day fever. In June and July sand-fly fever was epidemic. Many of the charts were typical of the different varieties of seven-day fever.

In 1909, 153 cases of "Pyrexia of Uncertain Origin," 3 cases of enteric fever and 470 cases of malaria were returned.

The monthly incidence of the pyrexia of uncertain origin and malaria was respectively as follows :—

	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
Pyrexia of Uncertain Origin	2	2	3	6	19	15	11	15	34	39	5	2
Malaria	30	18	19	32	53	62	81	68	40	25	25	17

The duration in days amongst the different cases of pyrexia of uncertain origin was as follows :—

Duration of fever in days	1 to 4	5 to 7	8 to 10	10 and over
Number of cases	87	49	14	3

On examination of the temperature charts, several varying from six to eight days' duration of pyrexia were characteristic of seven-day fever.

The temperatures of short duration were typical of sand-fly fever.

The large malaria incidence shown this year was due to the epidemic of that fever in India, the troops being infected before arrival at Aden.

In 1910, 92 cases of pyrexia of uncertain origin, 3 cases of enteric and 77 cases of malaria were recorded.

The monthly incidence of the pyrexia of uncertain origin was as follows :—

Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
0	8	7	8	2	9	21	20	5	7	3	2

Sandfly fever was very prevalent during July and August, but the temperature charts show several cases of seven-day fever between October and April.

In 1911, thirty-six cases of pyrexia of uncertain origin and thirty-five cases of malaria were recorded.

The monthly incidence of the pyrexia of uncertain origin was as follows :—

Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
5	0	0	13	3	3	4	3	1	3	0	1

In 1912, 29 cases of pyrexia of uncertain origin, 3 cases of enteric fever and 24 cases of malaria were recorded.

The monthly incidence of the fever was as follows :—

Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
2	2	0	0	1	4	4	3	3	6	2	2

During the years 1911 and 1912, seven-day fever does not appear to have been prevalent amongst the British Troops at Aden.

Through the courtesy of Captain M. D. A. Kureishi, I.M.S., I have examined

the hospital records of the 18th Indian Infantry, stationed at the Crater, Aden. From the arrival of the regiment on January 12, 1912, to December 31, 1912, 108 cases of pyrexia of uncertain origin were admitted to hospital; during June and July sand-fly fever was epidemic in the regiment, and during May and June the temperature charts showed that a few cases had suffered from seven-day fever.

The Disease Incidence, and its relation to the Temperature and Entomological Conditions.—There may be some relationship between the fever and the climatic temperature and the humidity of the atmosphere; possibly the connection is an entomological one. The fever appears about the end of April and is present until the end of September. There are no anopheles nearer than Shaikh Othma ten miles distant. *Culex fatigans* and *Stegomyia fasciata* can be found in small numbers throughout the year, chiefly breeding in shallow brackish wells, and in increased numbers from the end of May to the end of September when the fever is most prevalent.

INDIA FROM THE MEM SAHIB'S VIEW-POINT.

By Mrs. PERCY HOPE-FALKNER.

Being at home for a few months in the middle of a tour of service in India, one is constantly asked to give information regarding present-day home life, expenses, etc. In this brief article the intention is to write chiefly for those who are going out for the first time.

Any officer who is ordered out for a complete tour of duty receives "Indulgence," or entitled passages for wife and family, from the War Office, and there is little expense incurred beyond messing charges on board. These have to be paid for before starting, and one is usually sent P. and O., or transport of sorts, according to the "exigencies of the Service."

Roughly speaking, there are four or six cold days, three to four cool, and the rest of the voyage very hot. Plenty of changes should be brought for the journey, there being no means for laundry work being done, and an electric iron is useful as long as one is not found out. At least half a dozen changes of simple evening kit are necessary, bearing in mind twenty-two days of monotony of a kind, and long years of experience prove that several "cabin" trunks are more easily handled than large ones, and can frequently be wangled into one's cabin.

Arriving in Bombay is very bewildering for a newcomer—one is surrounded by yelling natives and pestered by English-speaking servants who want employment. It is most risky to take on one of these people without consulting some one who has been out before, as there is a regular trade done in fleecing a newcomer, and the more expert thieves usually wait till the Mem Sahib begins to "know too much."

There are two large hotels in Bombay, the Taj Mahal and the Majestic—both are expensive for the accommodation given, and the food is not very attractive in either. Both are usually quite full, and it is well to wire ahead for rooms.

The heat in Bombay is of the moist and clammy kind, and when the novelty has worn off, most people are glad enough to go on to their station. Conditions vary a little in every place, prices are slightly higher or lower, as the case may be,

but the following prices will be found to be fairly near the same everywhere, and even those prevailing in Jhansi, the very centre of India.

Houses.—Furnished bungalows are Rs. 50 to 100 per month according to the station, and there is always a shortage and always growling.

Servants.—Have been wiped out in thousands by the influenza epidemic, and are not, on the whole, nearly as good as formerly, but eventually one obtains a retinue at approximately the following prices:—

Butler	Rs. 30
Ayah	25
Cook	30
Kitmagar	25
Gardener	20
Syce	20
Cook's mate	10
Dhobie	25
Sweeper	10
Chokidar	10
Grass cutter	10

It is absolutely necessary for every lady to keep an ayah who will look after her room, clothes, etc. If this is left to the men servants, which happens all too frequently, the Mem Sahib loses caste in the eyes of the other servants. Even this small matter lowers the prestige of the white woman in India.

It is very rarely that one obtains a good servant under these prices nowadays, and the number one has to keep represents one's biggest monthly outlay in India.

Everything imported is very expensive, all tinned foodstuffs cost much more than at home, but butter, cream, tea, sugar, fruit, meat, etc., are absurdly cheap when compared with English prices. Good meat can be obtained in Jhansi, for example, for three annas a pound, a small leg of mutton being about 1s.

The cooks are usually excellent, and if one knows enough to show them new dishes, and supervise them thoroughly, they can turn out wonderful things. Nothing in the household should be left to the servants in that country of cholera and sudden death; whenever possible, all fruit and vegetables should be sterilized in permanganate, tables scrubbed daily, and all shelves and food utensils frequently washed in a weak solution.

Meat has been kept hanging three days in the hot weather by wrapping it in thin clothes wrung out in permanganate, which also helps to make it tender.

Sufficient furniture of a kind is usually obtainable locally in all Indian stations, but it is advisable to bring out anything possible, such as curtains, cushions, silver, linen, china, inexpensive pictures, etc. Leather goods are usually eaten by white ants, and Willesden canvas trunks should form the bulk of one's luggage.

Very good model frocks and really smart hats are obtainable in the more important places, but out of all proportion to their cost at home; therefore it is well to bring enough of these to carry on with.

The dirzy can usually copy anything wonderfully well, but he is not so good at picking up new ideas—though one can occasionally find one quite as good as any home dressmaker. They can always make chair covers, cushions, simple skirts, etc., even the worst of them, at a trifling cost, but one must always be present when "cutting out" is being done, or odd pieces will disappear in a most mysterious manner. Furs can always be used in the cold weather, and will last

all right if looked after. Glacé silk and taffeta are quite useless, and soon fall to pieces.

In nearly all Indian stations children do pretty well when small provided the necessary precautions are taken. There is the very vexed question of whether an ayah should be employed for sole charge of a child, and one hesitates to write on a subject on which one feels rather violently; but years of experience confirm the opinion that no real mother worthy of the name will leave her child in the sole charge of an ignorant native; unfortunately many hundreds do so in India rather than take the trouble themselves; children should be home at 7 years old at latest.

Most kinds of sports and games are available in military stations, and there is always tennis and some dancing. In Jhansi and other places where the club floors are good the dancing is excellent, and one can dance every evening. Ladies are in great demand, and there is usually a queue waiting for dances, which is just as it should be. Riding can be indulged in, but horses are expensive and scarce.

The hot weather must be spent in the hills—now an expensive undertaking—but necessary in view of the great difficulties of getting home, which still exist.

A few women try sometimes to "stick to it," but they become "crocks" sooner or later, and the very best line to adopt in India is to try hard to keep fit, and not try and see how much one can stand without becoming ill.

It was interesting to compare prices this tour with those of sixteen years ago, when account books had been kept and carefully preserved. Prices were so much lower then that one could live very comfortably on Rs. 500 a month, whereas now it needs careful management to do about the same on Rs. 1,000 a month.

This sum (say £120) provides one with far more than the same amount would in England, but one cannot live comfortably on much less, it being quite impossible if one keeps horses.

Even when one weighs all the disadvantages of climate, distance, etc., in India, it is preferable to serving at home at present from the Mem Sahib's view-point anyhow, if not always from the Sahib's.

Current Literature.

The Mycelial and other Micro-organisms associated with Human Actinomycosis. By Leonard Colebrook, M.B., B.S.Lond. (*British Journal of Experimental Pathology*, August, 1920).—The author regards as actinomycosis those cases which showed suppurative lesions, the pus of which contained granules visible to the naked eye, composed of a feltwork of filamentous micro-organisms. In restricting the use of the term to these cases he says he has practically adopted the standpoint of Homer Wright.

There follows a short account of the cases, and then he continues, both for diagnosis by films and for cultural purposes it has been proved necessary to isolate the actual granules from the pus. If the granules are not easily seen, shake up a small quantity of the pus in a test tube of water; all the ordinary elements of the pus are emulsified, but the granules remain intact and sink to the bottom of the tube, from where they can be removed with a pipette.

To verify mycelial structure a granule was lightly crushed under a coverglass

and examined unstained; for more detailed examination the granule was crushed more thoroughly, stained by Gram, and counterstained with weak carbol fuchsin.

To obtain cultures several granules were taken and washed in several changes of sterile water to get rid of contaminating bacteria, and then crushed in a drop of fluid between two sterile microscope slides; the culture methods were (1) glucose agar plates (PH about 7·4) incubated anaerobically by the palladium chloride method; (2) by pouring the inoculated agar into a narrow test tube and covering the top of the column with a layer of liquid vaseline or paraffin; (3) Dr. Mervyn Gordon's method of planting a granule in a tube of blood broth under oil, which promises to secure primary cultures with greater ease than either of the two first.

The author summarizes the first part of his paper as follows: (1) cultures of mycelial organisms were obtained from the granules of twenty-four cases of human actinomycosis; 21 of the 24 strains conformed in their general characteristics to the anaerobic type described by Wolff and Israel (*Actinomyces bovis*), and, later, in greater detail, by Homer Wright; 2 strains were also anaerobic but with slightly different cultural characters; and 1 was quite different —aerobic.

(2) All strains of *A. bovis* which were tested showed coarse agglutination with the serum of heavily infected patients. The serum of rabbits inoculated with the organism also gave a strong agglutination reaction.

(3) The current hypothesis that actinomycosis is directly conveyed to man from vegetable sources or from the soil is held to be probably false. Certain evidence is put forward which suggests that the organism is a common inhabitant of the human alimentary tract.

The second part of the paper deals with certain bacteria commonly found in close association with actinomyces. Actinomycotic granules are usually surrounded by an envelope of thickly packed leucocytes; if these leucocytes are washed away, and the granule stained by Gram's method and counterstained with weak carbol fuchsin, it will be seen that the Gram-positive mycelium is set on a background, which takes the counterstain and appears as a pink or red blur. This background is a densely compacted sheet of very minute Gram-negative cocco-bacilli, the separate organisms may be made out at the edge of the sheet, or where it is broken.

The organism is minute and may have the form of a micrococcus diameter 0·3—0·5 micron, or a very short cocco-bacillus 0·8—1·5 micron long. It is non-capsulated and non-motile. In cultures it grows aerobically and anaerobically on ordinary nutrient agar, glucose agar, or blood agar; the colonies are small, very adherent to the media, and very difficult to break up. Weak carbol fuchsin must be used as a counterstain as the organism does not stain with neutral red.

The author summarizes this part of his paper as follows: attention is called to the fact that, in addition to the mycelial feltwork always found in actinomycotic granules, there are frequently immense numbers of minute Gram-negative cocco-bacilli.

In eighty per cent of the cases these organisms have been found at some period of the disease; and in about a dozen instances they have been cultivated on artificial media. They are of unfamiliar type, and have not been met with in any other circumstances, so far as is known. It was proposed by Klinger, who reported the cultivation of similar organisms from four cases of actinomycosis in 1912, to apply to them the name of *B. actinomycetum comitans*.

The association of actinomycetum comitans with actinomyces in the granules is discussed but no satisfactory explanation has been arrived at. The findings are somewhat suggestive of a genetic relationship between the bacillary organism and actinomyces, analogous to that which Dunbar claimed to have demonstrated in the case of cholera-like vibrios and algæ.

Studies on Rickettsia Prowazeki. By Dr. R. Weigl, Professor of Biology at the University of Lemberg.

SUMMARY.

(1) By injecting into the intestinal tract of lice the least trace of leucocytes, taken from the blood of typhus patients in the pyrexial period, normal lice can be infected with *Rickettsia prowazeki* in each case.

(2) The same effect may be produced in lice injected with the blood of guinea-pigs which have been infected with the patient's blood collected during the pyrexial period.

(3) The etiological significance of the *R. prowazeki* the author had occasion to observe on himself whilst experimenting with lice (in 1917), in a typhus-free district, and having had no contact with typhus cases nor with carriers of infected lice for at least one month. The author scratched his finger, drawing blood, with the needle of a syringe loaded with a culture of *R. prowazeki*. After eighteen days a typical attack of typhus developed. Weil-Felix test was positive and typical skin lesions were found in sections of excised skin, while lice fed on the author during pyrexia became infected with *R. prowazeki*.

(4) Lice infected with *R. prowazeki* invariably succumb to this infection.

(5) The morphological character and in some degree the biological properties of *R. prowazeki* point to the bacterial nature of this organism.

(6) The invariably intracellular development of *R. prowazeki*, considered in conjunction with experiments on guinea-pigs, is the only available criterion of differentiation between *R. prowazeki* and other rickettsia.

(7) Last series of experiments carried out by the author indicate that the immunity of guinea-pigs to typhus is not a constant factor, secondary infections being fairly common, so that this immunity cannot equal in any way the immunity developing in human beings.

(8) The majority of authors do not indicate the strength of their vaccines. Before expressing final opinion as to the value of rickettsia vaccines it is essential that comparative tests be made with several vaccines each of a known strength.

(9) Only experiments on men can determine the efficacy of the protective vaccines prepared from rickettsia.

(10) The author has vaccinated several persons, but in spite of encouraging results (all the inoculated remaining free from infection during the observation lasting several months), he does not feel authorized to deduce any definite conclusions, as these men were living in conditions not especially exposed to infection.

(11) There was but a local reaction after the inoculations, and it never was severe in character.

(12) The vaccine was prepared in the following manner:—

The intestinal tract of infected lice was washed, after having been dissected with sterile precautions in saline solutions, then it was ground in a mortar with a small volume of saline solution. The bulk was then diluted in order to obtain an emulsion of the desired strength of rickettsia in each cubic centimetre, the number being 10,000,000 per cubic centimetre.

(13) The author gave three injections of this vaccine: first, 1 cubic centimetre, 10,000,000 rickettsia; second, after four days, 1 cubic centimetre, 10,000,000 rickettsia; third, after four days, 2 cubic centimetres, 20,000,000 rickettsia.

(14) Technique of examination for rickettsia: (*a*) Normal lice must be fed on patients in the earliest period of illness. A louse which has fed once on a typhus case becomes infected with *R. prowazeki*. When the temperature falls to normal *R. prowazeki* disappear from the blood. Lice are rendered intensely infective in eight to twelve days; (*b*) in order to show that lice become infected the examination of their fæces must be performed; (*c*) the identity of

R. prowazeki can only be proved in sections of whole lice or of the gut. The tissues should be fixed in formaline, or a mixture of formaline and potassium bichromate.

(15) Staining: (*a*) Two or three drops of Giemsa to one cubic centimetre H_2O acidified to the extent of two to four drops acetic acid per 100 cubic centimetres. This is allowed to act for two to three days. The stain must be changed two or three times; (*b*) rinse in water; (*c*) differentiation, if the staining is weak, with pure anhydrous acetone; if it is deep with acid absolute alcohol (ten cubic centimetres absolute alcohol plus two drops of acetic acid) then with pure absolute alcohol; (*d*) acetone plus xylol, eventually alcohol plus xylol-xylol-balsam.

The rickettsia appear as intensely dark blue spots on the decolorized background of plasma cells.

(16) In order to produce the artificial infection in lice the author introduces a glass tube, drawn out at one end to a very fine capillary and filled with infected material, through the anal passage into the anus of the louse. The capillary tube with the louse impaled is then fitted to a closely jointed syringe and the contents injected into the louse.

Thus the louse acts as an artificial culture medium and facilitates the examination for rickettsia, as well as the study of the rickettsia in cells and tissues.

The Present Position of Cancer Research.—The recent discussion at the British Medical Association meeting at Cambridge is well summarized in the *Lancet*, July 24, 1920, p. 205. Dr. Murray mentioned the very rigid criteria to which so-called cancerous growths must be subjected before their malignant nature can be accepted by the research worker. In the human subject the criteria are still mainly clinical. In animals probably the best criterion is to produce a secondary growth by transplanting an animal's own tumour to a part of its body away from the site of the primary growth. The Director of the Imperial Cancer Research Fund (Dr. Murray) is continuing the promising line of research opened up by these autologous grafting experiments. The outstanding achievement of recent experimental cancer research is Jensen's discovery that animals acquire a certain degree of resistance to secondary inoculation or grafting of the same on another carcinoma. The resistant state lasts only a short time. It is accompanied by the appearance of plasma cells in the connective tissues throughout the body, and according to some workers immunity is associated with an increase in the circulating lymphocytes. In rats and mice X-ray treatment in certain doses and exposure to a hot-dry atmosphere produce a lymphocytosis which is accompanied by increased resistance to implanted cancer. Dr. Simon Flexner agreed that a definite relation between lymphocytosis and tumour growth can be worked out, and that during the lymphocytic period animals are refractory to cancer inoculation. Dr. Mottram spoke of the different degrees of virulence of cancer tumours and of the different degrees of susceptibility of animals. Natural resistance is sometimes very high. Artificial resistance can be increased by various means, such as grafting embryo tissues and small doses of X-rays. But we cannot yet produce sufficient artificial resistance to protect completely all normal animals; and our methods of endeavouring to induce resistance artificially are at present too feeble to have any effect against spontaneous cancer. The *British Medical Journal* of July 31, 1920, p. 176, contains a summary of Sir Wm. Church's remarks at the annual meeting of the Imperial Cancer Research Fund. He described Dr. Cramer's experiments on the action of chemical substances on cancer cells in the test-tube and in the body. Salts of cerium were found to be the most active of those tested, manganese and uranium salts were less potent. But none of the substances tested had any effect on growing tumours. The failure is, perhaps, because the reagents do not gain satisfactory access to the cells, and

are rapidly eliminated by the kidneys and bowels. The difficulty of direct therapeutic experiment is also increased by the fact that the cancer cell is so like the normal cell of the body that agencies which destroy it are also dangerous to life. An essential preliminary to rational methods of treatment is a better knowledge of the vital processes in cancer cells and the differences between them and the normal cells. A beginning has been made with a study of cell respiration in connexion with this problem.

In considering the cause of cancer Dr. Murray suggested that we are faced with an alteration in the parenchyma of cancer cells, but then our knowledge is not yet sufficient to elucidate its nature. The *Bulletin de l'Institut Pasteur*, vol. xviii, No. 9, May 15, 1920, pp. 294 to 301, contains summaries of a number of articles, most of which deal with experiments on the production of cancer by chronic irritants. There is also an analysis of a paper by Professor J. Fibijer, of Copenhagen, who recently made the interesting discovery of cancer tumours in rats infected with a nematode worm (*Spiroptera neoplastica*) which passes part of its life in a cockroach. The staff of the Cancer Research Fund have received some infected mice from Professor Fibijer, and Dr. Leiper, Helminthologist to the London School of Tropical Medicine, is collaborating in repeating Professor Fibijer's work. Dr. Leiper has informed us that the only cancerous rats which Dr. Fibijer found to be infected with the worm in nature were collected from certain sugar factories in the West Indies, and that the cockroach which harbours the worm is a species whose normal habitat is the tropics. Present information indicates that no very striking results are likely to emerge directly from the observations made by Dr. Fibijer, but the work has directed attention again to a discovery made by Dr. Halland some years ago of a species of very small nematode in the mammary cancer tumours of old mice in England. This nematode is figured on p. 38 of the *Fourth Scientific Report of the Imperial Cancer Research Fund*, 1911, and Dr. Leiper has begun a study of its life-history.

Typhus.—"The "Anti-Typhus Campaign in Serbia, considered in connexion with the present typhus epidemic in Poland," by R. P. Strong, *International Journal of Public Health*, vol. i, No. 1, July, 1920. An informing account of the conditions in Serbia during the devastating outbreak of typhus in 1915, and of the measures adopted in the successful anti-typhus campaign. Strong considers his Serbian experiences to show that typhus epidemics can be held in check before any appreciable advance has been made in uplifting the people and changing their habits and mode of living. The epidemic in Serbia was entirely eradicated after six months' intensive work. The article, which is to be concluded in a future issue of the Journal, contains a brief summary of some noteworthy typhus outbreaks in the past.

Bacteriology.—"Irregular Typhoid Strains and the Infections caused by Them," by K. F. Meyer and N. M. Neilson, *Journal of Infectious Diseases*, vol. xxvii, No. 1, July, 1920. A description of laboratory infections (1) in a vaccinated caretaker exposed to laboratory animals excreting typhoid bacilli, and (2) in a vaccinated laboratory worker who was regularly working with strains of the *B. typhosus* group. The latter caused (3) a fatal house contact infection. From the blood of case (1) and from the urine of (2) an irregular atypical organism, and from the stool and urine of (3) typical typhoid bacilli were isolated. The irregular strains ferment (without gas) the usual carbohydrates, also dulcite, rhamnose, and irregularly arabinose. They rapidly cause an alkaline reaction in milk. In killed suspensions they are agglutinated by their own immune sera and also by *B. enteritidis* serum. As living organisms they are agglutinated by typhoid immune sera and by absorption tests can be classified as a subgroup of group III (Hooker). Antisera prepared with these strains agglutinate *B. typhosus* in living suspension only, and very slightly, if at all, *B. paratyphosus* A and B.

They resemble non-gas-producing strains of *B. enteritidis* from which they cannot be separated by absorption tests. The bearing of these observations on epidemiology, clinical aspect, and bacteriology of typhoid fever is discussed. The detailed study of irregular typhoid strains from the typhoid-vaccinated is important.

Small-pox Vaccination.—*Bulletin de l'Académie de Médecine*, lxxxiv, No. 28, July 20, 1920.—M. L. Camus contributes a paper, "A propos de la vaccination précoce des nouveau-nés," in which he directs attention to the well-known relative immunity of the newly-born infant to small-pox and vaccination alike. A vaccine which had a 100 per cent success rate for infants over 3 months of age only gave a success rate of fifty-three per cent for infants under 3 months. A good vaccine for infants over 3 months of age is, therefore, not necessarily a good vaccine for younger infants. It is possible to obtain a vaccine sufficiently potent to give a 100 per cent success rate even in children under 3 months of age: when such young infants are vaccinated, it is most important to make sure of the potency of the vaccine used.

Hygiene.—In the *Bulletin de l'Académie Royale de Médecine de Belgique*, xxx, No. 4, Séance du 24 Avril, 1920, Demoor and Slosse contribute a long article on "The Feeding of Belgians during the War and its Consequences." From the end of 1916 the daily ration was very inadequate, especially as regards proteid and fats. There was a marked increase in the prevalence of tuberculosis and rickets. The average weight of the infant at birth is less than before the war; the infantile mortality rate, however, decreased during the war: this was due to the almost complete disappearance of enteritis as a cause of infantile mortality. The Belgian population at the end of the war was extremely "run down."

(The statistics quoted in support of the author's contentions are not in all cases very convincing. Thus the death rates per *mille* for Brussels for the years 1913 to 1918 were: 14·5, 14·9, 13·9, 14·7, 18·3 and 21. The only years for which excessive rates were returned are 1917 and 1918. In these two years, especially the latter, influenza was prominent as a cause of mortality in Belgium as elsewhere.)

Beriberi.—"Beriberi in the Mesopotamian Force," by C. A. Sprawson, *Quarterly Journal of Medicine*, vol. xiii, No. 52, July, 1920. A study of the cases of beriberi that occurred in Mesopotamia during the war leads the writer to the conclusion that the disease called beriberi is a syndrome which may arise from various causes. One class of case is not due to a food deficiency, but appears to result from an infection. Other cases are due to a vitamine deficiency in the food: this takes a few months to operate in a previously healthy subject and may be called primary beriberi. In yet another class the syndrome appears to arise from the effect of some depressing influence or secondary infection in a subject previously rendered susceptible to the disease. These cases may be considered to have suffered from latent beriberi. In all classes the clinical appearances are approximately the same.

Malaria.—"Studies on Malignant Malaria in Macedonia," by Gaskell and Millar, *Quarterly Journal of Medicine*, vol. xiii, No. 52, July, 1920. In the course of a long paper which is evidence of a large experience of fatal cases of malignant malaria in Macedonia the authors conclude that the pathological changes of malignant malaria depend upon the toxin liberated by the parasite. The endothelium of blood-vessels, the brain, heart, liver and spleen are chiefly affected. The pathological processes which lead to death are of three kinds which correspond with definite clinical types.

(1) The true cerebral type, with signs of definite cerebral lesions and resulting paralyses; there are definite hæmorrhages in the white matter due to fatty degen-

eration of vessel walls. There is no great *general* increase of the malignant parasite throughout the body. Treatment is of no avail.

(2) A septicæmic type: intense general toxæmia—signs of cerebral irritation—coma; final rapid dilatation of the heart and failure. There is a rapid *general* increase of the parasite (asexual). When clinical condition fully established treatment of little avail. Parasite counts however give adequate warning; the limit of safety is 5,000 parasites per cubic millimetre.

(3) A cardiac type: cardiac failure without cerebral manifestations, caused by chronic degeneration of heart muscle; terminal general invasion of body similar to type (2) though less in degree. Treatment should be directed to cardiac condition with watch on parasite count.

(4) Intermediate forms between (2) and (3).

Polymorphonuclear myelocytes almost always present in severe anæmia of chronic malignant anæmia; this is of use in diagnosis when no parasites are to be found.

The complete cycle of development of the crescent from the ring has been followed in the brain of fatal cases of the true cerebral type.

Recent Work on Round Worm Infection. By F. H. Stewart, M.A., D.Sc., M.D. (from the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, June 18, 1920).—The paper commences with a geographical distribution and remarks on the clinical importance of Ascariasis in man. The average case is one of anæmia with lassitude, dyspepsia, and some muscular wasting. Taking into consideration the great frequency of the parasite, the amount of invalidity and loss of working power in the world at large from this cause must be very great.

The author, after these preliminary remarks, proceeds to the main thesis, viz., the mode of infection and the life-history of the worm. He describes the older work which proved that the segmentation and the formation of the embryo can occur in the outer world only. The upper layers of damp soil constitute the most favourable nidus. Moisture, a temperature above 60° F., abundant supply of oxygen and absence of putrefaction are essential. Experiments were carried out by feeding men, rats and dogs on ripe eggs and it was found that in some cases infection took place in the persons or animals experimented on. Mosler and Lutz, working with men, observed that dyspnœa with bronchitis and fever occurred some days after the administration of the eggs, which is very important in view of modern knowledge. At this time then the view held was that the worms were introduced into the definite host as embryos enclosed in eggs.

The author now proceeds to give an account of his own work done in Hong-Kong during 1914 to 1916. He first proved that infection could not take place from eggs through the skin. He then carried out feeding experiments on rats, and one of these dying of pneumonia some days after feeding showed on dissection that the lungs were intensely congested; on teasing out a bit of the lung in salt solution many nematode larvæ in active motion made their appearance, larvæ of a similar character were found in the liver. The results of further experiments on rats and mice brought the following facts to light:—

(1) Ripe eggs introduced into the alimentary canal hatch within twenty-four hours, this taking place probably in the small intestine.

(2) The larvæ issuing from the eggs bore into the wall of the intestines and migrate to the liver in forty-eight hours, probably going via the portal vein. They are found in the liver in the capillaries of the interlobular zone.

(3) About the same time they appear in small numbers in the lungs, and by the fifth day in large numbers. In sections they are found to be lying in the alveoli surrounded by a mass of red blood corpuscles. It is probable, therefore, that they reach the lungs in the blood-stream and act as emboli in the pulmonary capillaries. The numbers increase in the lung up to the seventh day and, if the

infection is massive, the lungs are solidified by hæmorrhage into the alveoli. A dose of five to ten thousand eggs will produce symptoms of pneumonia in a mouse or a rat.

(4) Larvæ pass up the bronchi on the sixth and seventh day and appear in the trachea on the seventh and eighth day.

(5) On the ninth day they begin to descend the alimentary canal, and passing rapidly through the œsophagus, stomach, and small intestine, accumulate in the cæcum, colon and rectum.

(6) They begin to pass out in the fæces on the tenth day.

(7) During the migration the larvæ develop greatly, they increase in size from 0·28 millimetre at hatching to 2 millimetres in the trachea and intestines.

This completes the life-history in the rat and mouse.

At this stage the author, having failed to produce infection by the eggs in pigs, guinea-pigs and dogs, thought that the rat and the mouse were the intermediate hosts and that infection of the definitive hosts, man and pig, took place by the ingestion of larvæ liberated in the fæces of these rodents. This conclusion he soon found to be premature, as early in 1917 he was able to demonstrate the same sequence of development in sucking pigs.

At this point the problem now consisted in tracing the transition from the larvæ in the lung to the adult in the intestine, since larval development could take place in the host of the adult worm.

The experiments now were interrupted, and although some further ones were carried out both at Hong-Kong and in Egypt to try and elucidate the further problem, the author did not seem to think that the results were convincing or the experiments sufficient.

Ransom and Foster, of the United States Department of Agriculture, repeated the experiments on rats, mice and pigs with similar results, and also found the same development in guinea-pigs and rabbits; they also followed it in a lamb and a young goat. In the lamb they found adult worms three months afterwards, and in the goat worms of ten millimetres after twenty-seven days.

They claim that these successes, in animals which do not frequently harbour ascaris, established the hypothesis of direct infection in one host only. Colonel Stewart thinks they are certainly very valuable evidence, but on the other hand he points out that failures to secure the appearance of adult worms in pigs are repeated, and, until the transition from larvæ to adult is followed out closely, no one can assert that further surprises are not in store.

Yoshida, publishing a paper in 1919, redescribes the migration of the larvæ in guinea-pigs and also in monkeys; he considers that the larvæ do not travel through the vascular system but through the serous cavities and directly through the solid organs. He applied an infected liver as a poultice to the nape of the neck of a guinea-pig and showed that the larvæ later on appeared in the lungs of the second animal.

One highly practical point remains to be decided, even assuming that development can take place in one host, namely, can infection take place from larvæ passed in the fæces of rodents?

The Apparent Rate of Disappearance of Diphtheria Bacilli from the Throat after an Attack of the Disease. By Percival Hartley, D.Sc., Captain, R.A.M.C. (T) and C. J. Martin, M.D., D.Sc., F.R.S., Lieutenant-Colonel A.A.M.C. (from the *Proceedings of the Royal Society of Medicine*).—This paper is based on 457 cases of the disease admitted into a Military Hospital for infectious disease at Rouen during 1917 and 1918.

Samples from the throat were taken by the same medical officer, the methods of examination were uniform, the diagnosis rested on the morphology and staining properties of the bacillus, and examinations were carried out on admission and

subsequently every seven days till three successive negatives were obtained. The day the patient reported sick was taken as the day of onset, and the time he apparently ceased to harbour the bacilli was computed to be the period half-way between the last positive finding and the first of three successive negatives. The authors, after these preliminary remarks, proceed to reduce the rate of disappearance of the bacilli to mathematics by means of graphs, and the following points come to light:—

(1) If a standard of three successive negative examinations is required the rate at which the carrier state apparently disappears is as follows: approximately five per cent. of those remaining each day become free from the bacillus in twenty-four hours.

(2) Generally speaking an individual who has carried the bacillus for a couple of months is just as likely to become free in the next few days as one who has carried for a week. This statement requires modification in the case of persons with abnormal throats.

(3) Three successive negatives at seven-day intervals does not exclude the possibility of discharging some few convalescents harbouring diphtheria bacilli, but this number is very small and may be represented by the unknown x.

(4) If only two negatives are required the time in hospital is shortened but the carrier rate is increased, and this is still further apparent if only one negative is required. The following table shows these points:—

Criterion	Percent discharged as free who are really carrying	Days in hospital
Three successive negatives	x	45
Two successive negatives	$x + 9{\cdot}3$	34
One negative	$x + 29{\cdot}0$	21

(5) In the case of convalescents with abnormally large tonsils and deep crypts who seem prone to become stubborn carriers, the authors agree with Pegler and Sears that the best treatment is the radical enucleation of the tonsils.

(6) A person who at the end of the week is free but at the end of the second week is carrying may not be a mere illustration of the experimental or sampling error of the method but may be the consequence of reinfection.

In the discussion that followed there appeared to be some doubt as to the value of bacteriological examination for the discharge of patients as based on the evidence of return cases.

Reviews.

Ophthalmic Operations. By Grimsdale and Brewerton. London: Baillière, Tindall and Cox, 1920. Pp. vii and 438. Price 18s. net.

This is the second edition of this book, which is one of the very best on the subject, and we can strongly recommend it to all interested in ophthalmic surgery.

The general arrangement of the subject matter is the same as in the previous edition. The operations are dealt with in a very thorough manner and they are lucidly described and illustrated.

A new section, on the surgery of penetrating wounds of the globe with retained foreign bodies, has been added. It embodies the improvements in treatment which have been adopted as a result of the recent war experience.

In the section dealing with the extraction of senile cataract it is interesting to note that in the authors' operation irrigation of the anterior chamber with normal saline is performed as a routine procedure for the removal of remaining

soft lens matter. This is a novel addition to the technique and they state it is not followed by iritis. The iridectomy they perform is of the basal buttonhole type after extraction of the lens.

We think the plan adopted in describing cataract operations, viz., after mentioning all the usual varieties of operation, and then describing one variety which the authors think the best, with the detailed procedure and the reasons for each step, is of great value from the student's point of view and might with advantage be extended to the other sections in which the ordinary set operations are described.

ELECTRIC IONIZATION. By A. R. Friel, M.A., M.D., F.R.C.S.I. Bristol: John Wright and Son, Ltd. London: Simpkin, Marshall, Hamilton, Kent and Co., Ltd., 1920. Pp. 78.

This little book dealing with a special department of electro-therapeutics is simply and clearly written, and is an excellent guide to those taking up the subject for the first time. It shows considerable originality, and the illustrations, none of which are copied from other books, are very good. If the author rewrites the book, it would be improved by some illustrative cases showing the results of treatment.

The book is excellently produced and printed, and remarkably free from errors. It can be strongly recommended as an introduction to the subject of ionization.

AIDS TO ELECTRO-THERAPEUTICS. By J. Magnus Redding, F.R.C.S. London: Baillière, Tindall and Cox, 1920. Pp. viii and 196. Price 5s.

It is a pity that Mr. Redding has chosen the "aids" series for his book; the student does not require it, the general practitioner has no use for electro-therapeutics and the specialist does not refer to the "aids" series for his reference. The material is good and it is easy to follow, and is in every way a very useful book.

May we advise Mr. Redding to write again, and then we feel that his book will probably be a standard work on electro-therapeutics? If he undertakes such a work we should advise him to leave out his chapter on X-rays, as he is taking on too large a branch of science on which so many special works have already been published.

RADIOGRAPHY IN THE EXAMINATION OF THE LIVER, GALL-BLADDER, AND BILE DUCTS. By Robert Knox. London: William Heinemann, 1920. Pp. 64. Price 7s. 6d. net.

This little book, which is reprinted from the *Archives of Radiology and Electrotherapy*, gives an excellent account of the present position of the value of radiography in the diagnosis of diseases of the liver and gall-bladder.

Without making any extravagant claims for radiography, the author shows that in a considerable number of cases, when taken in conjunction with the physical signs and symptoms, much help may be afforded to the physician and surgeon.

The experimental work, which is fully described, is interesting and has been carried out in a very thorough manner.

We have always been somewhat sceptical as to shadows on the X-ray plate which were stated to be due to gall-stones, but a perusal of this book shows that it will be possible in many cases, with improvement in technique, and further knowledge of the conditions of tube and exposure most suitable for this work, to rely on a negative X-ray as proof of the absence of gall-stones.

The book is beautifully illustrated and the reproductions of skiagrams are very clear.

It concludes with an abstract of the literature of the subject, which will be very useful to those desirous of going more fully into the subject.

The book is well worth study by all radiographers, and we hope it will serve to stimulate further research on this interesting subject.

MODERN ANÆSTHETICS. By J. Fedk. W. Silk, M.D. Second edition. London: Edward Arnold. Pp. 191.

The first edition of this valuable little book was published in 1914 and we feel sure that but for the intervention of the war this second edition would have appeared sooner.

The author states that the primary object of the book is to provide a simple guide for the student and practitioner in ordinary civil work, and it fulfils this purpose in a very complete manner. It is written in a lucid and attractive way, and is clearly the result of careful thought and long practical experience.

It is regretted that the subject of the relation of anæsthetics to shock could not have been more fully discussed and the dangers of chloroform and ether in this condition pointed out, together with the benefits that followed the almost universal introduction of gas and oxygen anæsthesia in conditions of shock during the War.

The remarks on shock on pages 37 and 38 hardly express the most recent work on this subject by Bayliss and Dale.

We entirely agree with the author's recommendations as to the preparation of the patient for operation under a general anæsthetic, and endorse the value of an undisturbed night before operation. The author is in some doubt as to the value of warming the ether vapour by means of a Shipway's apparatus and considers that the regularity of the supply and the lightness of the anæsthesia are the important factors.

However the result is obtained, those of us doing war surgery were fully convinced of its superiority over other methods of ether administration to serious cases.

A very good and reasoned account of the method of using intraspinal stovaine is given, and we would emphasize the importance of the administration of minute doses of ether as a preventative of the "psychic shock" which so often occurs if the patient is "present at his own operation."

Most of the bad reputation which this method gained during the War was due to faulty knowledge of the method and failures to prevent preliminary shock in arranging a seriously injured man in the position for lumbar puncture without first inducing light ether anæsthesia. When correctly used it is undoubtedly life-saving in high amputations of the thigh.

The termination of the book is somewhat spoiled by allusion to an old explanation of the causation of shock without reference to that important factor, namely, the loss of blood from currency by stasis in extensive capillary areas, which is probably the real cause of pathological changes in brain and other cells through deprivation of oxygen.

The book is well produced and illustrated and has an excellent index,

It can be strongly recommended to all interested in the subject of anæsthetics, as a full and impartial account of the methods, dangers and difficulties of this important section of the physician's art.

THE COURSE OF OPERATIVE SURGERY. By Victor Schmieden and Arthur Turnbull. London: Baillière, Tindall and Cox. Pp. xx + 350. 436 figures. Price 25s.

This book is a description of operative surgery as practiced on the cadaver and all the operations described are chosen with the object of teaching the anatomy of the part operated on.

Much less attention than is usual in a book of this nature is devoted to the

ligation of vessels and the classical operations and more space is given to operations on the abdominal viscera. While many of the old classical amputations have been omitted with advantage, yet those selected for description do not reflect the most modern teaching on the subject the result of the numerous amputations necessitated by the late War.

For instance: that most satisfactory amputation, a Syme, is dismissed in a few words, while a good deal of stress is laid on an operation such as Pirogoff's.

The book is really better as a surgical anatomy than as a description of the methods of performing operations.

In operations on the blood-vessels a good deal is said about the suture of vessels but no mention is made of Tuffier's tubes. We take exception to the advice given on page 103, that the bulb of a nerve should be first excised and then the nerve stretched before suturing. All stretching should de done before the removal of the bulbous end.

The anatomical descriptions are on the whole good and well illustrated but some rather vague descriptions are employed. Thus, the line for the subclavian artery is given as a line drawn from the larynx to the axilla, which admits of a large margin of error.

In the description of the ligature of this vessel above the clavicle, we are directed to strongly abduct the arm and clavicle outwards, a procedure which would materially add to our difficulty in reaching the vessel.

While the book is in some respects interesting and would serve as a good introduction to the subject for a student, it contains nothing novel and nothing that is not better given in numerous works on the subject by British authors. It is in no sense a book for the practising surgeon to consult.

The book is beautifully produced and is well printed and illustrated. We only detected one misprint, which is on page 92, three lines from the bottom of the page.

INTESTINAL DISINFECTION. With a Note on its Practical Attainment. By J. T. Ainslie Walker, Captain R.A.M.C.(T.F.). The Universal Medical Periodicals, Ltd. Price 6d. net.

This brochure of twelve pages brings to notice that the writer has improved upon his original benzene derivative—trimethol (*British Medical Journal*, February 26, 1916)—by one of a slightly different chemical constitution, dimethol.

Evidence is quoted to show that these drugs are ideal intestinal disinfectants. The latter has given clinical results which prove its superiority in practice even though its R.W. co-efficient is slightly less than the former.

"Here then we have at last a product that can be administered with the certainty that it will not only destroy bacteria in the intestines, but do so without absorption or toxic action, and which therefore should have a large and important field of use."

In the treatment of ulcerative dysenteries, acute and chronic colitis, and auto-intoxications due to intestinal putrefaction these drugs have proved effective.

Professor Tanner Hewlett, in a short introduction, says, "Dimethol has already been tried clinically with encouraging results, and if further experience confirms them intestinal disinfection is solved, and we shall possess a potent weapon wherewith to combat the many ills arising from alimentary toxæmia and intestinal sepsis." J. C. K.

THE MEDICAL ANNUAL, 1920. Edited by Carey F. Coombs, M.D., F.R.C.P., and A. Rendle Short, M.D., B.S., F.R.C.S. Bristol: John Wright and Sons, Ltd.

The ever increasing mass of medical and surgical publications makes it impossible for the busy physician or surgeon to keep abreast of all that is new in his profession.

The "Medical Annual" is a work which assists in overcoming this difficult problem, and year by year is one of the most valuable contributions to medical and surgical literature. The volume for 1920 ably sustains the reputation that the "Medical Annual" has made for itself. The names of the numerous contributors are a guarantee of the material contained in the volume. As usual a very wide range of subjects has been dealt with.

The important subject of vitamines is ably discussed, and the articles on deficiency diseases are worthy of special notice, but the whole volume is so rich in new ideas and material, that it is difficult to sum up the merits of the various contributions.

It also contains much additional information on books of the year, medical institutions, homes, spas, official and trade directory, medical and scientific societies and periodicals.

The publishers have done their work well and given us a handy volume, excellently printed and illustrated.

This is a volume which every practitioner should have in his library, and which no student presenting himself for the higher examinations should neglect to consult.

SURGICAL THERAPEUTICS AND OPERATIVE TECHNIQUE. By E. Doyen, in collaboration with H. Spencer-Browne, M.B.Cantab., etc. London: Baillière, Tindall and Cox, 1920. Pp. xix. + 811. Price 45s. net.

This third volume completes the English edition of Dr. Doyen's published works, and is a worthy companion to the preceding two volumes. This volume deals with abdominal operations, a subject on which Dr. Doyen is particularly at home, and it gives a very complete account of all the principal operations, and many of the minor ones which are often omitted from English text-books. The operative technique is described in great detail, but so clearly worded and so beautifully illustrated, that it is a pleasure to read. Some of the more important operations can be followed step by step on the illustrations alone, many of which are actual photographs.

It would be easy to select many points for criticism, but surgery has made such rapid strides in recent years, that it is not surprising that a large work of this nature, the publication of which has been delayed by the death of the author, and by the intervention of the European War, should in some instances fail to give the most recent opinion. But in spite of this it is of far more than merely historical interest.

Surgery on the Continent, and indeed all over the world, owes much to Doyen, and a large number of the operations described were originated by him. In fact it is more a description of his own methods than a treatise on contemporary surgery. Like most French works it makes very little reference to the work of British surgeons.

Dr. Spencer-Browne has carried out the difficult task of translation and preparation for the press in a most commendable way.

The publishers have presented the work of a great surgeon in suitable manner. The book is beautifully printed and the numerous illustrations are particularly good and clear. The book should have a place in every reference library.

THE X-RAY ATLAS OF THE SYSTEMIC ARTERIES OF THE BODY. By H. C. Orrin, O.B.E., F.R.C.S.Ed. London: Baillière, Tindall and Cox. Pp. 91.

This atlas consists of a series of X-ray plates taken from the cadaver after injection of the arteries with an opaque salt, so that the vessels are clearly shown.

Owing to the difficulty in obtaining adult bodies, the series of radiographs

were made from a full-term fœtus. Great care has been taken in indicating accurately on the plates the different vessels.

As might be expected the relative size of the vessels is at times misleading, depending on the distance of a particular vessel from the plate. This is well seen in Plate V, where the vertebral artery looks almost as large as the common carotid.

The plates are excellently taken and reproduced and display many points of interest.

Thus, the liability to gangrene following ligature of the popliteal artery is at once seen to be due to the small collateral circulation round the knee-joint.

The arteries only are dealt with and it is to be regretted that the author has not included some plates to show the cranial sinuses, as such skiagrams are most helpful to the surgeon.

Both the student of anatomy and the surgeon will find this atlas very useful.

The publishers have succeeded in producing a very handsome little book, with excellent reproductions of the skiagrams and clear letterpress.

GONOCOCCAL INFECTION IN THE MALE. For Students and Practitioners. By Norman Lumb, O.B.E., M.B., B.S.Lond., M.R.C.S.Eng., L.R.C.P.Lond. London: John Bale, Sons and Danielsson, Ltd. Pp. 328. 165 figs. and 13 coloured plates. Price 25s. net.

Owing to the great attention which is at present being devoted to the prophylaxis and treatment of venereal diseases, it is not surprising that the demand for books on the subject has increased.

During the last six months several have been published, including an excellent little book by the present author on "The Urethroscope in the Diagnosis and Treatment of Urethritis." The present volume, which is a more ambitious one, and includes much of the work and excellent illustrations already published in that little book, is certain to be extensively read.

In dealing with a disease like gonorrhœa, in which complications are such an important factor, correct deductions as to frequency and their incidence under various treatments is only possible when the number of cases dealt with is large. The author amply fulfils this condition, as he refers to notes of 50,000 cases which have been under his personal care.

He rightly lays great stress on the use of the urethroscope as an aid to diagnosis, particularly in the chronic type of case which resists the ordinary lines of treatment.

The book makes no extravagant claims as to the success of any particular line of treatment, but gives an excellent account of the routine measures which he has found most efficient in dealing with a very large number of cases.

The case for vaccines is fairly stated. The author considers that they are of value in the treatment of gonorrhœa, and diminish the likelihood of complications. Definite rules for the administration of vaccines are laid down.

As might be expected, a very considerable section of the book is devoted to the complications of the disease.

The book concludes with some excellent hints regarding the points which will help the practitioner in deciding when the patient is cured, and rightly insists that a single negative examination is not sufficient. We would go further than he recommends, and be very cautious in pronouncing a patient cured as the result of a second negative examination at the end of three months.

The book is clearly and simply written, and can be confidently recommended to the practitioner as a sound treatise on the present position of our knowledge of this serious disease.

It is excellently produced by the publishers, and the illustrations, particularly those in colour on urethroscopic appearances, are very good. The book has a good index.

Correspondence.

TACTICAL HANDLING OF FIELD AMBULANCES.

TO THE EDITOR OF THE "JOURNAL OF THE ROYAL ARMY MEDICAL CORPS."

SIR,—Major Reed has certainly opened up a most interesting if not vital controversy as to the tactical handling of field ambulances in mobile warfare.

My knowledge of the subject is limited, and my views are the result of experience gained on the Salonica front, where operations were mainly restricted to trench fighting. When the "break through" occurred, such success was gained that an armistice was arranged before there was opportunity of testing our tactics in mobile warfare for a prolonged period. Our subsequent forced march through semi-hostile Bulgaria, to threaten Constantinople, was not associated with active operations.

The points which Major Reed has put up, I take it, are :—

(1) Should a field ambulance be a brigade unit commanded by the colonel commandant of the brigade, or,

(2) Should it remain as a divisional unit, commanded by the A.D.M.S. of the division as heretofore, or,

(3) Should it be sometimes one, and at other times the other?

As regards the first, Major Reed points out that under such conditions the field ambulance would come into line with the R.A.S.C. train company and the field company R.E. As a result, at any rate, on paper, there would exist a complete group of units commanded by, in a phrase, "the man on the spot."

The field ambulance commander would be in close touch with the brigade staff and consequently would receive early information of events happening and likely to happen. But, should he not have the time or opportunity to be close to the man on the spot, owing to pressure of work in the field ambulance, unless the medical service were represented on the brigade staff by the permanent appointment of a medical staff officer, I think he would be as badly left, if not more so, than certain field ambulance commanders were, owing to paucity of orders from the A.D.M.S. Moreover, the brigade commander and his staff cannot have sufficient technical knowledge to control effectively a medical unit. Again, the "get 'em in and get 'em on" principle of the fighting man is diametrically opposed to the "get 'em out and get 'em back" idea of the medical officer.

I don't think personally that the brigade commander is the right man, though I must confess that I found the G.O.C.'s brigades most helpful, and keen to facilitate the work of a field ambulance during operations, yet they could not be expected to look upon operations from the same point of view as a medical officer, consequently the medical services, in the long run, would suffer.

Perhaps the advocates of the brigade school derived their views from some conditions which have limited their field of thought. Those conditions are, I think, as stated in a later paragraph.

As regards the second consideration. The principle of assigning the command of a group of medical units to one who is "one of themselves," a "whole-timer," and has had much previous experience acquired in the units he is designed to command, seems to be the right one. An A.D.M.S. thinks of his field ambulances

by day and dreams of them by night; he has not ten thousand other matters which interest him more and about which he knows more, to attend to. Give me the right man on the wrong spot, in preference to the wrong man on the right spot.

As regards grouping and co-ordination of the field ambulances in action, were they not divisional units, what unnecessary labour and correspondence would ensue should a "brigade field ambulance" be required to operate outside the sphere of action of its own brigade!

Major Reed lays down a most important truth, in my opinion, when he states that "deficient and defective liaison was at the bottom of most of the 'incidents.'" A field ambulance commander very soon realizes the vital importance of liaison.

A distinguished senior officer under whom I have had the honour to serve for a considerable period, considers the problem of field ambulance work under three headings. The first is transport, the second is transport, and the third is transport; perhaps we should add "liaison" and read "transport cum liaison."

There is no doubt in my mind that the "incidents" were due to individual failings, circumstances beyond the control of any individual, or to lack of liaison, and not to a system under which the A.D.M.S. commands the medical units in a division.

It would be a pity to destroy a system of command which on the whole seemed satisfactory and which could be adjusted where it showed weakness, and substitute one which in my opinion is fundamentally wrong. Could not we, therefore, adjust "the defective and deficient liaison" that Major Reed talks about? Could we not arrange for the communications which we ought to have and have not? A certain field ambulance commander on the Western front did have proper communications and trained telephonists. He was, I am told, most successful, and there were no "incidents" involving his unit. Perhaps he would speak. Something more than a motor of sorts, a tired horse, or his own flat feet, are required by an A.D.M.S. or a field ambulance commander to ensure that "incidents" do not occur.

The third consideration suggests that when a brigade is acting independently of the divisional staff, and detailed so to act, a field ambulance should be a brigade unit, but I think a medical officer should be detailed to act on the brigade staff to ensure liaison. There is no doubt in my mind that, as Major Reed states, this should be laid down very definitely in "Field Service Regulations, Part II."

In my endeavour to defend the system which existed during the late War, perhaps I am prejudiced by the happy experience of serving under A.D's.M.S. who appreciated liaison and never spared themselves physically or in any other way to ensure to the utmost of their power that the field ambulance commander was informed of the situation and instructed precisely as to what means should be taken to deal with it.

I am, etc.,

C. L. FRANKLIN,

Capt., R.A.M.C.,

Lately commanding a Field Ambulance with the B.S.F.

DESTRUCTION OF MOSQUITO LARVÆ.

TO THE EDITOR OF THE "JOURNAL OF THE ROYAL ARMY MEDICAL CORPS."

DEAR SIR,—In the JOURNAL OF THE ROYAL ARMY MEDICAL CORPS, for November, you published an interesting paper entitled "The Value of Small Fish regarding the Destruction of Mosquito Larvæ," by my friend Major Boyd, in which he shows that the sticklebacks in the dykes around Sandwich consume anopheline larvæ.

Referring to a paper of mine entitled "The Question of Natural Enemies," published in the Journal for March, 1920, in which I maintained that only under unnatural conditions were natural enemies of real value and practical importance as a means of controlling anophelines, Major Boyd cites the finding of anopheline larvæ in the stomachs of the sticklebacks as evidence that they are an important natural control. Now I admitted in my paper that the fish in the dykes were "voracious larvæ eaters," but even so, the bionomical balance in such natural conditions as the dyke system is such that there are countless thousands of anopheline larvæ in the dykes in spite of the presence of swarms of fish. Anyone who has visited Sandwich with a view to ascertaining the concentration of anophelines will readily admit that they abound in that locality. How then does the fact of finding larvæ in the stomachs of sticklebacks justify the statement that they are an important means of control?

Similarly we might argue from finding flies in spiders' webs that spiders are an important means of controlling the house-fly. The enemies of insects destroy large numbers—sometimes very large numbers—but under entirely natural conditions a balance is set up, and the enemy by no means has everything in its favour. Major Boyd later on in his paper says "When the weeds have been cleared from the dykes the advantage will be on the side of the fish, and they will probably prove of more use than even at present," which in other words, I think, substantiates my contention that under unnatural conditions only are natural enemies of some practical value in controlling the development of anophelines.

I am, etc.,

MALCOLM E. MACGREGOR.

Wellcome Field Laboratory,
Wisley, Surrey.
December 17, 1920.

Notices.

EDITORIAL NOTICES.

The Editor will be glad to receive original communications upon professional subjects, travel, and personal experiences, etc. He will also be glad to receive items of news and information regarding matters of interest to the Corps from the various garrisons, districts, and commands at home and abroad.

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Original Communications.

ON AN EXPERIMENTAL INVESTIGATION OF *SPIROCHÆTA DUTTONI*, THE PARASITE OF TICK FEVER.[1]

[*Reprinted from the Lancet.*]

BY MAJOR-GENERAL SIR WILLIAM B. LEISHMAN, K.C.M.G., C.B., K.H.P., F.R.S.
Director of Pathology, War Office.

IT is my first and a very pleasant duty to thank you most sincerely for the high honour you have paid me in inviting me to deliver the Horace Dobell lecture, and I am further deeply in the debt of the Royal College for their courtesy in permitting me to postpone its delivery on several occasions since the date originally fixed in 1914. Not only has an interval of years elapsed since I carried out most of the experimental work which I shall describe, but I have been unfortunate enough to lose some of my records and sketches, which disappeared during the period of great stress under which the great work of the Vaccine Department of the Royal Army Medical College was carried on. Enough, however, remains to enable me to put before you some hitherto unpublished observations, many of them verified by my re-examination of microscopic specimens, while I am also glad of the opportunity of revising my work as a whole in the light of much that has recently been done and written on the same subject, or on others with which it stands in intimate relation.

The subject of the pathogenic spirochætes is one in which I have always taken a deep interest, and during the last fifteen years I have devoted a large part of my free time to their observation. Those with which I have worked, at one time or another, have been *Treponema pallidum* and the spirochætes associated with yaws, Vincent's angina, phagedænic

[1] The Horace Dobell Lecture delivered before the Royal College of Physicians of London on November 2, 1920.

tropical ulcer, and those responsible for the different varieties of relapsing fever. The largest part of this work has been devoted to the last-named group of organisms, and in particular to the African variety—tick fever—caused by the *Spirochæta duttoni*, and I have on several occasions published the results obtained at various stages of my inquiries. The subject has expanded so enormously of late years, and touches, or is touched, on so many sides by researches on other spirochætal infections that it must be my endeavour to speak as generally as may be and to introduce detail only where this is called for in illustration or support of some essential point. Anything of the nature of a historical account of the experimental investigation of tick fever and of its cause, the *S. duttoni*, would be quite impossible within my limits of time, and for the same reason I must touch but lightly on the valuable work of many observers in many lands, even when this work appears to call for detailed comment on account of its criticism of some of my own. I trust this may be borne in mind if I appear not to do full justice to the observations of any particular worker.

I propose to deal with my subject on the following lines: first, with a condensed account of some of my earlier work; secondly, with work which has either not been published or only briefly mentioned; thirdly, with the work of others on the same or closely related branches of inquiry which appears to have a bearing upon the life-history of *S. duttoni*.

Early Work.

Differentiation and Cultivation.

Some of my earliest work on the subject was a study of the morphology of the spirochætes of the different relapsing fevers, and an investigation of the differentiation of the European form, due to *S. recurrentis*, from the African form, due to *S. duttoni*.

I studied these two spirochætes from material obtained from Fraenkel and kept alive by passage through mice. Both their animal reactions and morphology were compared and contrasted with the experience recorded by others. I need say no more on this point than that the impression I then formed has been strengthened by my later experience. This was that it is a very difficult if not impossible task to differentiate these spirochætes by any morphological characteristics owing to the great variety of forms and size which one encounters in specimens taken at various stages of an attack and by varying the method of collection, fixation, and staining. Almost all of the points usually quoted as distinctive of one or other species I have encountered within a single species by varying the conditions just mentioned. I would speak almost as strongly with regard to differences founded on the animal reactions of the strains. These I have found, in the case of the strains with which I have worked, to be very inconstant; and although, personally, I have done but little in the way of the cross-immunization of laboratory animals I am

not inclined to attach great importance to these in view of the individual differences I have encountered in the degree of immunity conferred on monkeys and mice infected in my experiments with *S. duttoni*. The uncertain factors of dosage and the individual resistance of the animal must, I think, count largely in the results of such cross-immunity experiments.

The same remarks apply to the other strains of relapsing fever, which have from time to time been described, and it cannot at present be asserted with any degree of confidence how many varieties there are of either the African, the European, the Indian, or the American forms. All that I think it is possible to say at present is that the human relapsing fevers are all due to spirochætes which cannot with certainty be distinguished one from the other by morphology or by animal reactions, and that they probably owe such differences as we find in them to the influences of locality and to differences in their arthropod vectors. In this I agree with the views expressed by Fantham.

A Phenomenon of Aggregated Spirochætes.

I need perhaps hardly say that I, like most other workers on these elusive organisms, have spent much time on attempts at artificial cultivation of the spirochætes. I have not met with anything that I can regard as a success, although on one occasion I was able to maintain the organisms alive and motile, as well as of proved virulence, for a period of fifty-one days by employing as a medium a mixture of nutrient agar and a broth prepared from the bodies of medicinal leeches.

My observations of the prolonged vitality of the spirochætes in these animals and the interesting changes which they underwent in them was my reason for employing this unusual material of culture. Still, successful transplantation from tube to tube failed here, as always in my hands. At the same time I should like to put on record that I have once observed *in vitro* in one of my cultivation experiments, conducted with citrated mouse blood maintained at a low temperature, a phenomenon which has left me with a very strong hope that truly successful cultures of these organisms may yet be obtained. In this specimen I observed not only an undoubted and great multiplication—that has been often noted—but the living and intensely motile spirochætes had aggregated themselves into most beautiful rosettes, precisely similar to those with which we are familiar in cultures of trypanosomes and leishmania. The perfectly regular radiate arrangement of these rosettes and intense rotatory movements of the individuals comprising them excluded any possibility of the arrangement being one of chance or degeneration.

History of Tick-ingested Spirochætes.

My experiments were, however, in the main directed towards the fate of spirochætes ingested by the tick, the mode of infection by tick bite, and

the manner in which hereditary transmission of the organisms takes place in the tick. At the time I commenced there appeared to be little doubt upon many of these points since the work of Dutton and Todd and others of the earlier investigators, and, later, that of Koch, appeared to make of it a simple and obvious story.

Koch, for example, had traced the spirochætes from their passage through the walls of the tick's gut into the body cavity and organs of the tick and found them in large numbers in the ovarian tissue; there they penetrated into the young ova, where they could often be seen in numbers. They increased rapidly as the development of the larva and nymph proceeded, until, as he said, they were eventually masked by the growth of the tissues of the young tick.

Without in any way questioning the accuracy of these observations I was for a long time unable personally to confirm them. After several failures to secure infection from the earliest batches of ticks sent to me by brother officers from Africa, I attributed this simply to the ticks not being infected, and was confirmed in this by my complete failure to detect spirochætes in any of them. When finally I did receive a batch whose bites infected a monkey I was, however, surprised to find that here, too, I could find no spirochætes in any of the ticks of the batch which I dissected. It was, of course, possible that infectivity was limited to one or two of these ticks, and that those I selected for investigation were uninfected.

However, as my experiments progressed with the known infected ticks, with which I was then able to provide myself by feeding them on animals suffering from relapsing fever, I still found it extremely hard to find any trace of spirochætes in the body of a tick fed on heavily infected blood later than the tenth day after the feed. Similarly laborious searches in hundreds of eggs laid by heavily infected ticks, or dissected out of their ovaries, were also completely negative, and although in a subsequent communication I was able to record that spirochætes had eventually been found in three eggs, these were eggs of ticks which had been kept at comparatively high temperatures, and even under these conditions a visible infection of the egg with spirochætes was an extremely rare phenomenon.

While these experiments were in progress I had been struck by the frequent occurrence in various parts of the body of the ticks of curious little clumps of granules, staining deeply with the reaction of chromatin, and highly refractile. The individual granules were usually rod-shaped and resembled minute bacteria, often with a diphtheroid-like beading or segmentation; at other times they were spherical or oval. By appropriate staining or illumination it was often possible to demonstrate that individual clumps of granules were contained in a definite and approximately circular matrix, usually unstainable, but sometimes very faintly tinged with blue by my stain. These granules were extremely irregular, both in their numbers and their distribution in different ticks, the commonest site

being within the cells lining the Malpighian tubules and in the ovarian tissue. I shall not spend longer on their description, since their appearance and distribution have been recounted in my earlier communications, and they are familiar to others who have worked on the same subject. They are also fairly well demonstrated in the microphotographs which are shown.[1]

From the first I suspected these granules of being parasitic, and of having some connexion with the spirochætes, so naturally my inquiries thenceforth were very largely connected with attempts to determine whether or no this was the case. Like most of those who have worked with this organism, I was interested in the curious changes which the spirochætes ingested by the tick undergo in the stomach of that animal. These have been described and figured by many besides myself, and the segmentation of the chromatin core of the spirochæte, as well as the appearance of lateral or terminal buds, are well known. These changes you may follow in the sketches which I have made from *S. duttoni* and other spirochætes.[1] I had myself before this made a close study of these changes in spirochæte blood kept under various conditions *in vitro*, and had gained a very strong impression that they were not degenerative, as they were usually held to be, but must serve some purpose in the life-history of the organism.

Bearing this in mind I was impressed by the frequency with which identical changes were encountered in the spirochætes ingested by the tick when the gut contents were examined from day to day. Further than this, I remarked in many ticks that the almost complete disappearance of the spirochætes from the stomach of the tick often coincided with the appearance in that situation of great numbers of short rods or granules giving the chromatin reaction. Their resemblance to bacteria was considerable, but all attempts at cultivation failed, and I came to the conclusion that they were the segments of the chromatin of the ingested spirochætes which had either been extruded by them when living or set free by their death. Careful dissections of ticks made with a view to study this point showed that in many cases, if not in all, there followed some days after the ingestion of heavily infected spirochæte blood a great increase of the granule clumps in the body of the tick, chiefly in the Malpighian tubules and the genital tissues.

Difficulties encountered during Investigation.

In connexion with this observation, and also in respect of the greater part of these investigations, I would lay stress on an unavoidable limitation of one's work on ticks, which has the uncomfortable result of substituting conjecture for the certainty for which one might hope as a result of the painstaking and thorough investigation of a given point.

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[1] Not reproduced.

Owing to their structure and nature it is only possible to determine the presence or absence of anything for which one may be in search by sacrificing the tick and examining all the organs, tissues, and fluids; this search cannot, therefore, be made on the same tick from day to day. Some have attempted to get over this by snipping off a leg—by which one obtains a sample of the cœlomic fluid—or by incising the dorsal chitin and cutting off or aspirating the contents of one of the prolapsed gastric diverticula; but such procedures appear to me very unsatisfactory, especially when negative results are recorded, in view of the extreme irregularity of distribution of both the spirochætes and of the bodies which may conceivably be derived from them. In consequence, one has to employ the only alternative—to deal with one's nymphs or adults in batches which are fed at the same time and submitted to identical experimental conditions, and then to dissect one or more daily, trusting that the picture presented by the individual may be representative of that in the other members of the batch. I may perhaps be pardoned also if I remind you of the labour necessary to carry through such an experiment as the daily investigation of members of two or three batches of ticks submitted, for example, to different grades of temperature before or after feeding. Their dissection, the preparation of specimens of the various organs and tissues, and the prolonged microscopic study of these make heavy demands, and yet it is work which is not worth the doing unless one is prepared to devote to it the time required. In illustration of this I may mention that I have on several occasions had to revise my conclusions on a particular experiment as a result of a second prolonged search through a series of films.

On the other hand, I may claim that in most instances, indeed in all of the more important ones, I have repeated the particular experiment several times, the results thus controlling one another and safeguarding one from the drawing of hasty conclusions.

Mode of Infection.

Early in my work I was able to show that the probable mode of infection in tick fever was not, as had been usually assumed, through the inoculation of the spirochætes from the salivary secretions through the biting parts of the tick's mouth, but through the penetration of the infected secretions, passed by the tick while gorging, into the wound caused by the bite. One of these secretions, the coxal fluid, had, I found, pronounced anti-coagulating power, and this facilitates the entrance of the virus if it should be present, as is undoubtedly the case at times, either in it or in the other fluid voided by the tick, the white secretion of the Malpighian tubules.

This was demonstrated by an interrupted feeding experiment, in which a number of ticks were allowed to bite a monkey and after they had fed some minutes, but passed no secretions, they were gently removed and placed on a second monkey, on which they finished their meal and passed

freely their secretions. The first monkey was not infected, but the second contracted a severe and typical attack, while a mouse inoculated with some of the voided secretion also contracted the fever. The experiment has since been repeated by several other workers who have confirmed my result. At the same time another attempt of my own to repeat it failed, inasmuch as neither monkey was infected, nor was the mouse inoculated with the secretion, and this in spite of the fact that a spirochæte was found on searching the centrifuged secretions used for the inoculation of the mouse.

I do not question that at times infection may occur through the bite alone of the tick; indeed, I have myself found spirochætes in the salivary gland, though only on one occasion. The granule clumps also are occasionally seen in the salivary cells, though neither as frequently nor in as great numbers as in other situations. Such a mode of transmission is, I fancy, less common in the actual infection of man than the entrance of the virus held in the secretions through the wound caused by the bite.

I have found that infection is by no means a certainty even when spirochætes are subsequently found in numbers in the tick which was employed, and, conversely, I have on very many occasions, I believe the majority, found no trace of a recognizable spirochæte in the ticks concerned when a successful infection has followed on the bite of individuals which I had myself infected at various periods by allowing them to gorge on infected mice or monkeys.

Influence of Temperature.

These irregular results were the rule and not the exception in the case of ticks maintained at a moderate temperature, not exceeding 25° C., but different results were obtained when they were kept at higher temperatures, either for a few days or for more prolonged periods.

I varied the conditions here on the assumption that one might be more likely to reproduce the results obtained by Koch and others, who worked in the endemic zone of tick fever, by approximating to the conditions of temperature there obtaining. A very large series of experiments were done to determine the influence of higher temperatures both on the infectivity of the ticks and on the spirochætes which they had been allowed to ingest. One was encouraged to proceed with these by finding, as one soon did find, that the ingested spirochætes behaved in an unexpected and very suggestive manner when the ticks were kept at temperatures ranging from 25° to 37° C. These changes were of two kinds, and to each of them I attach considerable importance.

First, the granule clumps I have described as being commonly encountered throughout all stages of the tick's life, from the intra-ovarian egg onwards, showed very often, under the influence of warmer surroundings, a very definite change of shape; from being mostly small rods or ovoids, as I have described, increasing numbers of them were found to

have assumed a circular or coccoid form. They appeared to me also to have increased in numbers, but on this point it was not possible to be certain for the reasons I have already given. In the case of some of these granules I think this change was preliminary to their subsequent development into what I may speak of as "young spirochætes." I was never successful in observing the development of these young spirochætes from granules in ticks prior to their having been fed on spirochæte blood in the laboratory; but in ticks which were placed at the higher temperatures subsequent to a feed on infected blood the same changes were found in the granules, and in this case, as I shall recount later, I have seen such development.

Secondly, a very remarkable difference was found on following from day to day the fate of ingested spirochætes in the bodies of ticks fed at the same time on the same animal but subsequently divided into two or three lots, which were kept at different temperatures. Five of these experiments were carried through, involving many months of laborious work, and the results were of sufficient regularity to allow of the following general description.

At temperatures below 25° C., the spirochætes maintain their motility, characteristic shape, and staining reactions for three or four days; after this they rapidly become motionless, distorted in shape, tend to aggregate in tangles, and show very irregular staining. In the days following, these changes become more pronounced and it is increasingly difficult to find an unaltered spirochæte until, on or about the tenth day after the feed, they are found to have disappeared entirely from the gut. I mentioned earlier the liberation of the segments or granules of chromatin from the altered spirochætes and the synchronous apparent increase in the number of the granules encountered in the Malpighian tubules, the generative organs, and elsewhere. No further changes were observed, though individual ticks of the batch were dissected and examined, sometimes months after the termination of the experiment. At the same time it is never safe to assert, at least in my opinion, that a given tick which has once been fed on infected blood, or has been born from an infected mother, and possibly also the descendant of an infected grandmother, is free from infectivity, for I have now and then encountered an odd spirochæte or possibly a small tangle of them in some situation when prolonged search of the specimens from this tick and from others belonging to the same batch had, up to that time, been completely negative.

Turning now to ticks kept after feeding at temperatures above 25° C. Here it was found that comparatively little change occurred in the spirochætes during the first two or three days after the meal; thereafter they underwent the same changes as have been described for the ticks kept at the low temperatures, but apparently with greater intensity and greater rapidity. By the eighth to the tenth day after the meal active unaltered spirochætes had either vanished completely from the tick's body

or were extremely hard to find. But—and this is the interesting point—at or about this same period there was a sudden reappearance of spirochætes in various tissues, but spirochætes of an altogether different type—small, delicate, faintly staining, and less regularly curved than those found in the blood. When first seen they were usually present in enormous numbers and showed no increase in the days following, rather a slow decline. It gave a strong impression of a simultaneous development or origin rather than of a rapid process of multiplication from a few individuals. They were found mostly in two situations: in the walls, not the lumen, of the receptaculum of the stomach and of its diverticula, and in the cells lining the Malpighian tubules. When liberated from these situations by teasing or crushing, and kept in a suitable medium, they showed active motility. They varied in length from individuals the size of a cholera vibrio to others almost as long as the blood forms. These "young spirochætes," once they had made their appearance, tended to persist in the ticks, and in most of the experiments in question I was still able to find them, often in great numbers, many months after the tick had been removed to the cool incubator.

Another interesting point which was noticed in several of these experiments was that the young spirochætes appeared in successive waves at intervals, roughly, of seven to ten days, as long as the ticks were kept at the higher temperature. The suggestive bearing of this observation upon the successive crops of organisms which synchronize with the febrile relapses in man and animals will be obvious.

Diminution and Reappearance.

Although the subject is one which does not lend itself easily to illustration by graphic methods, I have endeavoured in the charts (figs. 1 and 2) to show the course of events in several of these experiments as regards the number and character of the spirochætes encountered in the dissected ticks in the days following the infective feed and their being placed at the respective temperatures recorded. You will see that the charts bring out the following points:—

In the three batches of ticks kept after infection at temperatures below 25° C., which may be considered as controls, the spirochætes diminished in numbers with great rapidity, and although a few odd ones were encountered up to the end of the period of examination they did not reappear in any numbers. On the other hand, in the five batches which were maintained at temperatures above 25° C., after the feed on spirochæte blood it will be seen that, following on the initial disappearance, there is a remarkable reappearance of the organisms, usually an abrupt change in which they increased from a few isolated specimens to great quantities, which in some cases largely exceeded the numbers found at the first examination. But the change is not limited to numbers; these are not the same kind of

spirochæte, being almost wholly those small, fine, and irregularly curved forms which I have spoken of as "young spirochætes," and they are almost entirely confined to the tissues and are not at this stage free in the body fluids or the lumen of organs. The sites in which I have most frequently found them are in the walls of the gut, in the cells lining the Malpighian tubules or between these cells and the delicate membrane which forms the external coat of the tubules, in the ovarian or testicular substance, and, finally, within the sarcolemma coating the striped muscle

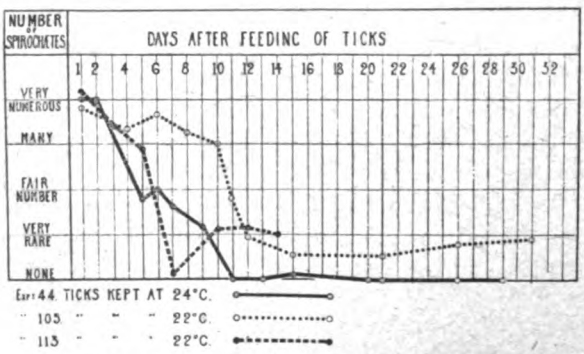

FIG. 1.—Ticks kept at temperatures below 25° C.

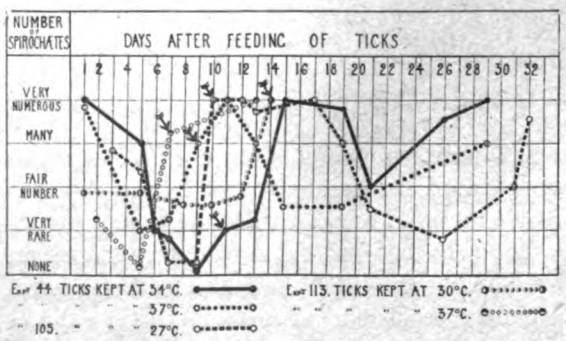

FIG. 2.—Ticks kept at temperatures above 25° C.

fibres. Naturally, in crushes of organs many escape and are found free, but I am convinced that they are formed within the tissues—probably from the granule clumps—and that it is only at a later stage and under certain conditions that they grow to full size, escape into the fluids of the body, and wander at their will. In order that you may follow the course of events more clearly, I have, in fig. 2, indicated by arrows the points at which these young spirochætes were first detected, and all readings later than that refer to this variety and take no account of the few fully developed forms encountered, which may either have persisted from the original infecting dose or have developed out of the younger forms.

More Recent Work.

This brings me up to the point of my more recent work, if one may so speak of pre-war labours, which now seem very far away. The observations of which I have hitherto spoken were almost entirely made upon specimens dried, fixed, and stained by my own method. Staining was always carried to a maximum degree of intensity, and the film subsequently cleared of every trace of deposit by weak alcohol or by acetone. Examinations as to motility were made from time to time in moist specimens, but were not employed as a routine measure for the detection or enumeration of the spirochætes.

Dark-ground Method.

The great advantages of the dark-ground method had in the meantime come into prominence, and I determined to repeat certain portions of my work, using this method of illumination as my routine, and I had constructed for me a special thermostat in which my microscope might be placed, so that specimens could be observed continuously at any temperature selected. By this technique I repeated a number of experiments, including those I have just commented on, in which infected ticks were maintained and contrasted at different temperatures. No essential change was made out in respect of the number of fluctuations of the spirochætes, and the series investigated in this manner are included in the charts just described.

The technique, however, was more fruitful in other directions. Great attention was paid to the appearances of the spirochætes and of the granules under this method of demonstration, and the finer details of structure shown by staining were contrasted and correlated with the pictures shown on the dark ground. Much was learnt from this, and the combination of these two methods of study is a very helpful one, as each aids the other and confirms or corrects the impressions founded upon one alone. I have found that it is even possible to make good use of the dark-ground method on stained films. Any structure, the details of which have been studied in the stained film, may be clamped in position on the stage, and the other illuminating system substituted without disturbing it. It will be found that a very satisfactory dark-ground picture is obtained, the details of the refraction of the structure showing out as well as in a moist preparation, and being only slightly affected by the tinge of colour given by the stain. By employing this method it was possible, for instance, to clear up doubts which might exist as to a certain granule or other structure, the refractility being of great assistance in determining its true nature.

As regards the spirochætes themselves, I was chiefly interested in trying to make out some further details as to the characteristic formation of segments and granules from the homogeneous chromatin core contained

within the periplast of the adult and unaltered parasite, and also to observe further the appearance and structure of the terminal or lateral buds. As I have already mentioned, I had seen these both in attempted cultures of *S. duttoni* and other spirochætes, and also in the body of the tick. The segments and grains into which the chromatin core divides are readily seen in living specimens thus illuminated, and the grains in particular are highly refractile. They are often observed in spirochætes which show at the time intense motility, and are thus clearly not a post-mortem change. As to the shedding of these granules, described by Fry, Balfour, and others, I could not personally confirm this, for although I have watched a granule vigorously coursing up and down a spirochæte as its rotation reversed, and then seen it apparently ejected into the surrounding fluid, I have also seen the same granule return, in all appearance, to the body of the spirochæte and resume its perigrinations. This I attributed to some foreign particle being caught in the vortex currents set up by the rotation of the spirochæte and being set free when these movements changed or ceased. But although I failed to convince myself of their extrusion in the case of the spirochætes which I kept under observation with this object, I believe that eventually they are extruded, either while it is still active or when it is quiescent and in appearance dead. It is difficult to know what appearance may be taken as indicating the death of a spirochæte; for instance, many have observed and described the empty sheaths which are often found in exhausted cultures and other situations; by this method of illumination these show a very pretty double outline in place of the even and homogeneous refraction of most of the active forms. But, I have also seen such double-contoured forms in active movement. Again, spirochætes kept *in vitro* for many days at temperatures approaching the freezing-point may show no trace of motility on examination, but on placing them on the warm stage I have seen great numbers become once again actively motile.

Lateral or Terminal Buds and Granule Clumps.

The lateral or terminal buds, too, were closely examined. They contained one or more granules of chromatin, very highly refractile and variable in size and shape, embedded in a matrix which gave a faint milky radiance, like that of protoplasm, but somewhat more hyaline. At times the bud was seen to be pedunculated and attached merely by a very thin filament to the spirochæte. Spirochætes possessing such buds in all stages were often as active as those which had none, so this, too, is no evidence of a degenerative or post-mortem change. Detached buds were also seen on many occasions, and many of these could not be distinguished by either method of examination from some of the granule clumps found elsewhere in the tissues of the ticks. The sketches which I show you will save the need for further description (fig. 3).

The granule clumps themselves were examined from many situations, and here the chief point made out was that the capsule or matrix, of which there was occasionally an indication in stained films, was more often observed, and the intensely refractile granules were seen to be embedded in a milky matrix of approximately circular and well defined outline.

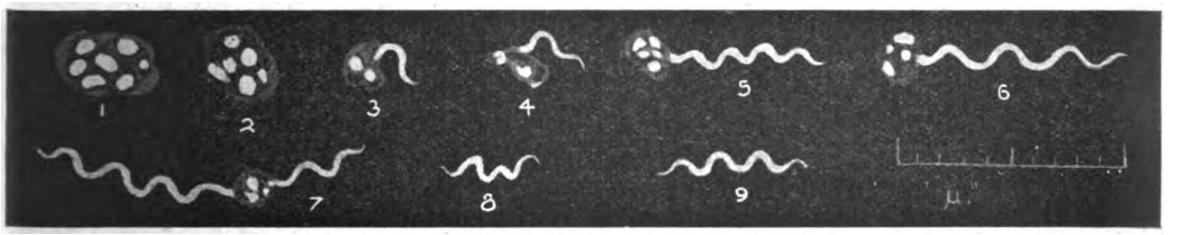

FIG. 3.—*Spirochæta duttoni*. Sketches of living forms of young spirochætes observed on the warm stage by dark-ground illumination.

1, 2, Granule clumps. 3, 4, Growth of young spirochætes from granule clump. 5, 6, Longer forms. 7, Growth from each side of clump. 8, 9, Young free spirochætes.

Search was made by the same method for altered spirochætes or for granules in the bodies of infected mice at various periods during the first attack, the fever-free period, and at the beginning and end of a relapse. Much of interest was observed, too detailed to describe beyond saying that I found granule clumps in the spleen, particularly in the spleen at the beginning of a relapse, which appeared similar to those found in ticks. It is, however, impossible to assert that they were identical, since so many other granular bodies are found normally in the same situation. I also noted some very minute spirochætes in association with granules in this situation, similar to those found in heated ticks.

Observation of Circular Bodies in Spleen.

I refer, however, to those observations chiefly to record that it was here, in the spleen of an infected mouse at the commencement of the first attack, that I encountered some curious bodies, of whose nature I am uncertain, and which I had not encountered elsewhere in stained films, either from mice or ticks.

By dark-ground illumination these bodies were seen to be perfectly circular in outline, varying in diameter from about six to twenty microns, and showing an even and delicate milky refraction. Within each body were small spherical granules, from 0·5 to 1 micron in diameter and intensely refractile. There were usually three or four of these, seldom more than six. The most curious feature of these bodies, however, was the extreme motility of these dazzling little granules, which darted from side to side of the containing sphere with amazing energy, and would have formed an

admirable illustration of the movements of electrons within an atom. They were chiefly found in the spleen, but a few were also seen in the liver.

Their interest in connexion with the line of my inquiries was greatly increased by my subsequently encountering them in the bodies of infected ticks which had been kept after feeding at a high temperature—the condition, it will be remembered, under which young spirochætes make their appearance. To the eye the bodies were absolutely identical with those found in the spleen of the mouse, exhibiting the same refractility and the same intense motility of the contained granules. Stained specimens of the same material gave no evidence of them, doubtless because the granules only would stain, and their irregular arrangement with reference to one another would give no suggestion of a common matrix or capsule. In the experiment No. 113, which was one of those included in the composite fig. 2, these bodies were found in ticks of the lot kept at the highest of the three temperatures, 37° C., and in them alone. They were first noticed two or three days before the other ticks of the batch showed the usual rapid reappearance of spirochætes of the young type.

The next observation of these bodies was in connexion with an experiment, No. 111, of a different nature.

Here three adult ticks, members of a batch whose bites had infected a mouse on the occasion of their last feed, were now allowed to feed singly on separate mice, with a view to ascertaining which were still infective, and in order that any eggs subsequently laid by a tick of known infectivity might be studied. In this experiment two of the three mice were infected, the other remaining well. Subsequently, each of these ticks was dissected and the fluids and tissues examined by the dark-ground method; in each of the ticks which had proved to be infective these same curious bodies were readily detected, none could be found in the other tick. Granule clumps of the usual type were found in each tick, but a prolonged search disclosed no recognizable spirochætes.

Finally, six adult ticks, which had been bred in the laboratory and had before fed on infected blood, were again allowed to gorge on a heavily infected mouse. They were then placed in a bottle, which was kept in a water-bath at a temperature of 30° C. Sixteen days later they commenced to oviposit, and on examining some of these eggs four days later, both by staining and by dark-ground illumination, these same bodies were again seen by the latter method. No spirochætes were found.

At this point I was obliged to interrupt my inquiries, so I am still unable to do more than record the appearance of these bodies and the situations and circumstances in which I encountered them; but I think it will be admitted that the observations are suggestive of their having some connexion with the spirochætes. I refrain, with some difficulty, from speculations as to the probable nature of this connexion.

Apparent Growth of Spirochætes out of Granule Clumps.

My final reference to the dark-ground observations relates to the apparent growth of young spirochætes out of the granule clumps, but as this has already been recorded and figured in my last article, published in the *Annales* of the Pasteur Institute, I shall only recall that I found these forms by continuous observation of the crushed tissues or of the fluids of infected and heated ticks with the microscope kept in a thermostat at a temperature of about 30° C. The sketches reproduced in fig. 3 will save further description of the forms seen, and it need only be added that all the forms figured were extremely motile. For some days before these forms had been seen spirochætes had either been absent or extremely rare in other ticks similarly treated, while immediately after the observation of the forms figured the tissues of the remaining ticks were found to be swarming with the young forms to which I have so frequently alluded.

Observations of Other Workers.

I come now to the consideration of the observations made by other workers, either on the organism of tick fever or upon the morphology and life-history of other spirochætes. The volume of the work in question has already grown formidable, and it would be quite impossible for me to give of it anything approaching a full and critical review in the time left me. The utmost I can attempt is to mention some of the more essential portions of this work which bear directly upon my own experience and views, as these have been presented to you, and to examine in how far the observations are in agreement or discord. In doing this I trust my earlier remarks may be borne in mind, and that the brevity to which I am constrained may be my apology for the very inadequate and incomplete account which I must give of much that is of importance and, to myself, of great interest.

I think I may best deal with this work by discussing it under headings corresponding in order, as far as may be practicable, with the various parts of the investigations I have just described.

(1) *The Morphology of the Spirochæte.*

There is, on the whole, little divergence of opinion in this direction, at all events as concerns the adult organisms found in the blood of man and experimental animals or studied in attempted cultures.

Many have described its structure as far as this is disclosed by various staining methods and by observation of living specimens. The fragmentation of the chromatin core, which may be taken to represent the nuclear apparatus, and the frequent differentiation of this into definite rods or granules, highly refractile and showing the staining reaction of chromatin, has been universally observed, and excellent descriptions, as well as good coloured plates, have been published. The work of Dutton and Todd, of

Breinl, Fantham, Hindle, Carter, and many others leaves no doubt that these changes occur. As to their significance, however, there is not yet agreement. I think it may be said that my British confrères, almost without exception, consider, as I do myself, that the change is a vital one and connected with the life-history of the organisms, but others hold that this is still unproven, while some, such as Marchoux and Couvy, regard it as an early stage of degeneration. Such a view as the latter would appear to be supported by the undoubted fact that the beading and segmentation of the chromatin is, as they have pointed out, a pronounced feature in spirochætes which are placed in unfavourable surroundings, as, for instance, in cultural experiments in which, whatever degree of initial success is obtained, the organisms eventually die off. This, however, I do not think need necessarily be held as evidence of its being a degenerative change, as we have many examples in microbiology of the formation of resting forms or of the earlier stages of a secondary cycle when the organism finds itself so unfavourably placed as to be in danger of dying out.

(2) *Number of Species of the Relapsing Fever Spirochætes.*

Little need be added here. The recent literature of spirochætosis is full of accounts, mostly clinical or epidemiological, in which the type of fever encountered has been considered by the writer for one reason or another to be distinct from any of the three which are pretty generally accepted—viz., those due to *S. recurrentis, duttoni,* and *carteri.* More than one type of African relapsing fever is believed to exist, and others have been described in Palestine, in Persia, and in Mesopotamia. I think that all that can safely be said at present, for the reasons I mentioned earlier, is that while such varieties are very probable it is not yet possible to define with any confidence specific differences between the causative organisms.

(3) *Artificial Culture.*

Success has been claimed in this direction by Levaditi, by Duval and Todd, and by Noguchi, but only the last claims more than a temporary success, the cultures dying out after a few passages. At the same time, it is of great interest to know that these spirochætes can not only be kept alive, but can be got to multiply abundantly *in vitro,* if only for a time.

Interesting points emerge from the study of such cultures, and I have been struck by statements in connexion with several of the methods that the spirochætes were noticed to show a certain periodicity in the vigour of their multiplication, fresh crops of active organisms appearing at intervals of some days. Very small spirochætes were reported also as being found in some cases; for example, Levaditi speaks of "formes vibrionennes," which sound to me extremely like my young spirochætes, although in my own attempts at cultivation, in which the spirochætes were kept living and virulent for fifty-one days, I did not encounter small forms similar to those

met with in heated ticks. Finally, nearly all who have worked with spirochætes *in vitro* note the frequency of the granular change in the organisms, as well as the lateral and terminal buds of which I shall speak later. Noguchi, in his classical researches on the cultivation of spirochætes, has noticed in several instances the occurrence of a granular phase ; in the case of *S. phagedenis* he states that the granules when liberated appear to remain alive and at certain periods to develop into spiral forms. Similar granules were found by him also in cultures of *Treponema pallidum*, and he has stated that it was the finding of these which led him to re-study sections of paretic brains for the presence of this spirochæte, with results with which you are all familiar.

(4) *Occurrence and Significance of Granules and Buds.*

Numerous observations have been made which bear on this point, either directly or indirectly. The actual formation of the granules and the observation of their origin from the spirochætes has been noted not only in connexion with *S. duttoni* but with many other spirochætes of widely differing habitat and mode of life.

I cannot pretend to give an exhaustive list, but may mention the following, in addition to the group responsible for the relapsing fevers of man : *S. gallinarum, S. bronchialis, S. theileri, S. phagedenis, S. anodontæ,* and *S. balbiani, T. pallidum* and *T. pertenuis.*

In almost all of these the granular phase which has been recorded appears to follow very much the same lines, even in species so widely removed from one another in habit as the spirochætes of mammals and birds and those of Lamellibranchs, such as *balbiani* and *anodontæ.* The process of their development and liberation from the spirochæte have been very precisely described and figured by both Fantham and Bosanquet, and many of their observations are so closely in accord with my own upon *S. duttoni* that we might almost have been describing the same specimens.

On this point, therefore, I think it may now be accepted as a generalization that spirochætes as a class tend at one stage of their life to form small granules which are subsequently liberated from the periplastic sheath. A similar statement may also, I think, be made in connexion with the curious buds or swellings which form upon spirochætes either terminally, subterminally, or laterally. These, too, have been observed by so many workers and in connexion with so many different spirochætes that their existence must also be taken as proved, whatever view be held as to their nature.

To turn now to the significance of the granules on the one hand, and the buds on the other. Here we are on less certain ground. My own view, as you are now aware, is that from some of these granules or buds a new generation of young spirochætes may, under favourable conditions, arise. As regards the views of others, I think my best procedure will be

to put before you very briefly the principal arguments or observations which have been urged against what I may term the "vital" theory of their nature. Later I shall refer to work of a confirmatory nature.

It has been urged that the experiments of myself and others on infectivity, either through the bites of ticks or by the inoculation of tissues or secretions of ticks which showed no spirochætes, must, when infection resulted, have been due to our failure to observe spirochætes, which in reality must have been present. This is the view held by Marchoux and Couvy, by Blanc, by Kleine and Eckhard, by Wolbach, and by Wittrock. In most cases they reach this conclusion as a result of finding spirochætes in their own experiments in the majority of cases in which the tick-bites or the inoculum proved infective. On this point I have never been so foolish as to claim that I could be certain of the absence of an odd spirochæte; but I cannot admit that I, and others who have had the same results, have in the experiments in question overlooked them through faulty staining methods or inadequate search. Further, I do not think that Marchoux and Couvy, who are the chief exponents of this view, add to the cogency of their criticisms by assuming the existence of an "invisible" phase of the organisms to account for the temporary absence of spirochætes which they, too, have noticed in the bodies of ticks, some days after feeding on infected blood.

German workers—Wittrock, Kleine, and Kleine and Eckhard—have chiefly repeated and extended Koch's original investigations in East Africa on the presence of the spirochætes in ticks which they had proved to be infective, and have confirmed Koch's observations as to the presence of recognizable spirochætes in the eggs of Ornithodorus. For them this accounts satisfactorily for the known facts of transmission and of the hereditary passage of infection, and they do not consider that any further stage of development of the spirochætes is required to explain these facts. In some of their work, and that of others as well, irregular results have been encountered, as all have encountered them, but I am not in sympathy with the explanation sometimes given that these failures to infect are to be attributed to the individual immunity of the experimental animal in some cases or of the particular tick in others. They have also carried out a series of experiments similar to those which were successful, in the case of trypanosomes, in proving the existence of a phase of non-infectivity in the tsetse fly. The results being negative, they conclude that no such cycle occurs in spirochætes.

Many have raised, and very properly raised, the objection that granules similar to those found in *Ornithodorus moubata* are encountered in a number of other ticks and other Arachnids. Marchoux and Couvy in particular describe and figure those they have seen in six different species of ticks and in *Laelaps echidninus*. Although the granules figured in some of their plates do not appear to me to resemble those I have been describing, I have no doubt that others do. Of other Argassine ticks

which I have myself had the opportunity of examining—viz., *O. savignii*, *O. tholozani*, and *Argas persicus*—only in the last-named did I find granules which, though differing in many points as regards their arrangement, relative numbers, and distribution, appeared to me similar to those found in *O. moubata*. But the Argas in question had been employed in some experiments in the transmission of *S. gallinarum*, and the relation of this spirochæte to the granules found in the tissues of Argas has been the subject of elaborate studies by Balfour and others, many of which are confirmatory of my own experience with *S. duttoni*. I may add that the closely allied *O. savignii* with which I worked proved non-infective to mice, but in one instance when I fed one upon a mouse whose blood contained *S. duttoni* I did find a few granule clumps subsequently in the Malpighian tubules, the only case in which I encountered them in this species; I would not, however, lay much stress on this as my material was very limited.

It has further been suggested, for instance by Bétancés, that the granules are capable of being interpreted in another fashion as pre-secretory or as mitochondria, but many points in connexion with their distribution in the tissues and fluids of the tick appear to me strongly against such an assumption, and I have on more than one occasion encountered adult ticks in which I could find no trace of them.

What is undoubtedly puzzling is the great number of these granules occasionally observed in the Malpighian tubules or genital tissues of ticks which, even if they had acquired an hereditary infection, had never fed on spirochæte blood during their life. As the numbers of granule clumps found in the intra-ovarian eggs is never large it is obvious that the granules can increase in numbers without any fresh spirochætal infection. Assuming for a moment that the vital theory is correct it seems certain that they are therefore capable of multiplication in the granular form, and probable that their development into spirillar shape is an exceptional occurrence brought about by influences not as yet fully determined.

Turning now to the support to be obtained from confirmatory observations, many of my earlier experiments have been repeated and extended by Nuttall, Fantham, Hindle and Todd, to mention only those who have dealt with *S. duttoni*, and I must limit myself to referring you to their published work, merely adding that I do not think I misrepresent these workers in saying that they conclude from their own experiments, as I do from mine, that the granules are derived from *S. duttoni*, represent a vital process in the life of the spirochæte, and are neither degeneration products of these organisms nor granules derived from the cells of the host.

Fewer observations have been made on the significance of the buds so often mentioned. The majority have, I think, held them to be degenerative changes, while Todd, who concludes that the granules are vital and can give rise to a new generation of spirochætes, does not consider that this is the case with the buds. They are, however, so conspicuous and

definite in their form and so uniform in structure, whether this is studied in stained films or in moist preparations by dark-ground illumination, that I feel that their further study is most desirable. At the present moment I am inclined to think that they are the precursors of some of the granule clumps, and I have an impression—I am not in a position to put it more strongly—that the clumps from which I have seen the young spirochætes developing were of this nature, rather than such as owed their origin to the fragmentation and extrusion in granular form of the chromatin core of the adult spirochæte.

(5) *Observations in Recent Literature upon "Young Spirochætes."*

I have naturally searched the recent literature pretty closely for observations which might bear upon the forms which I have called "young spirochætes." While some state that they have seen no development of the granules into spirochætal form, others record having seen this happen, or mention observations which are at least capable of being interpreted on the assumption that such a change has actually taken place.

Dutton and Todd themselves stated, as far back as 1907, that it was apparently possible to trace the development of granules into comma-shaped masses of chromatin, and of those into small spirochætes, while if the "cysts" described by Breinl about the same time were of the same nature as the granule clumps in question, then he, too, considered these structures as originating in spirochætes, and as being capable once more of giving rise to them. Levaditi, in the cultural experiments already mentioned, in which he placed collodion sacs containing infected blood in the peritoneal cavity of rabbits, says that towards the end of the experiment very small forms, "formes vibrionennes," were seen, actively motile, pointed at both ends, and containing one or two grains of chromatin. I have also alluded earlier to Duval and Todd's cultures, and the appearance in these of an alternate increase and diminution of the number of spirochætes seen, an observation suggestive of successive crops of new individuals.

Bosanquet, in his work on *S. anodontæ*, records the finding of very short forms, and Balfour, in commenting on this work, mentions that he had found very similar forms, undoubtedly developing from granules, in the Malpighian tubules of *Argas persicus* infected with *S. gallinarum*. Fantham, working with *S. bronchialis*, states that the granules which are derived from them have been seen in the tick to elongate and assume a sinuous form; he observed the emergence of very small spirochætes from the group of granules.

In addition to such positive evidence it appears possible to extract a little of the same nature even from the work of some of those whose researches have led them to conclusions altogether adverse to the views I have put forward. For example, Marchoux and Couvy, in speaking of the effects of temperature on the possible developmental cycle of *S. duttoni*, record an experiment in which they could find no evidence of spirochætes

in a tick which had been kept at a moderate temperature; but after placing this tick at 28° C. for two days they noted the appearance of numerous small and actively motile spirochætes. Although they would no doubt offer a different explanation for this, I think it may well have been an example of a development of a crop of young spirochætes as a result of the higher temperature, similar to what I observed in the experiments I have described to you. In another part of their work they confirm my observation of the granules, when kept at 37° C., developing into bacillary or even vibrionic form, though not into true spirochætes. Kleine and Eckhard, also, who worked in Tanganyika, and in general confirmed Koch's work in German East Africa, mention their encountering in ticks collected from the native quarters spirochætal forms as small as cholera vibrios, though they were unable to say whether they were degeneration forms or were capable of growing to full size.

These observations constitute a body of evidence which it is not easy to set aside, and I feel that if I have erred in the conclusions which I have drawn from my own observations I err in excellent company.

(6) *Influence of Temperature.*

There are a number of points relative to the influence of temperature upon the development of the young forms of spirochætes in recent work upon *S. duttoni, S. gallinarum* and *S. recurrentis.*

In the first place a large part, perhaps most of the work in question, was done in the tropics or subtropics, where the temperatures, though no doubt showing seasonal variations, must, on the whole, have approximated to those which I employed artificially with the help of the incubator and water-bath. At all events, the temperature at which my stock of ticks was kept—21° to 23° C.—can rarely have been touched. To me this suggests a highly probable explanation of the discrepancy in the results recorded by such tropical investigators and those which have been obtained by myself and others whose work on this subject has been done in a climate which is politely labelled temperate. I do not for a moment question the results of Koch, of Kleine and Eckhard, and others who found, in Africa, a high percentage of infective ticks, and who record the ease and frequency with which spirochætes were detected in ticks whose bites proved infective to animals, and in the crushed organs or the fluids of ticks which, when injected into animals, infected them. This, I think, is quite what one might expect, assuming the change into the young form to be dependent upon a certain height of temperature, and probably upon some other less readily-appreciated climatic conditions. Our devices in imitation of these natural environmental conditions have, no doubt, from the tick's point of view, been crude enough, and may well be responsible for the comparative rarity of what I may call positive results.

The "formes vibrionennes" of Levaditi's cultures were obtained at the

high temperature of the peritoneal cavity of the rabbit, a factor which may have had a bearing upon their appearance. Hindle, also working with *S. duttoni*, repeated much of my work, and found that while infectivity appeared to be limited to the gut-contents, sex-organs, Malpighian tubules, and excrement of ticks maintained at 21° C., in those which he kept at 35° C. all the organs and tissues, including the salivary glands, were found infective. He notes, also, a shorter incubation period in mice when material from the heated ticks was used. He found no spirochætes in the organs of the 21° C. ticks, but when infected ticks were heated for two or three days at 35° C. he saw, as I did, the reappearance of spirochætes in the gut and the organs of the ticks, as well as in the cœlomic fluid. Fantham, by keeping ticks' eggs at a temperature of 34° to 37° C. for four to six days before inoculating their contents into animals, was able to infect, respectively, fowls with *S. gallinarum* and mice with *S. duttoni*, and he also noted microscopically the development of granules into bacillary forms. In a later communication he adds that when infected eggs were kept at 37° C. for five days the larvæ which subsequently hatched from them were seen to harbour typical spirochætes, while he was also able to follow all stages in the development of the coccoid forms into elongated bodies and eventually into typical spirochætes. Further, he found that the inoculation of the contents of eggs containing granules alone was rarely followed by infection unless they had been previously heated for a few days at 35° C.

Nicolle and his colleagues, of whose important work on the transmission of *S. recurrentis* I shall speak in a moment, mention that the lice with which they experimented and in which they noted the reappearance of spirochætes were kept in a warm chamber at 28° C., a fact which may quite possibly have had an important bearing upon their results. From Marchoux and Couvy's work may also be extracted some observations which seem to support the significance of the temperature factor in such experiments. I have already referred to the instance in which they found numerous very small and active spirochætes in a tick which had been kept for two days at 28° C., but in which they had previously failed to find them. In speaking elsewhere of the influence of fasting on the presence of spirochætes in Argas, they say they found them in abundance in the cœlomic fluid in ticks of this species which had been kept for forty-five days at 28° C. Kennedy, working at Baghdad, presumably at a high temperature, on lice removed from relapsing fever cases, found in addition to the buds formed on the ingested spirochætes a number of exceptional small spirochætes in one part of the body of the louse. Lastly, Borrel and Marchoux, working some years ago with *S. gallinarum*, stated that this spirochæte developed rapidly in Argas at a temperature of 35° C., but that this did not take place at temperatures between 18° and 25° C.

Without laying too much stress on any individual observation, especially in view of the fact that in some instances the observers' attention was not

directly fixed on this matter of temperature, I think it is justifiable to take them as a whole as affording considerable support to the view that a relatively high temperature has a most important influence on the development of these spirochætes in their arthropod host, and also upon the infectivity of the latter.

(7) *Corroborative Work upon Relapsing Fever.*

In view of its importance I have left till the end a brief consideration of the recent work of Nicolle and his colleagues at Tunis, much of which has been substantiated by parallel observations made in Algiers by Sergent and Foley. This work, although carried out upon the parasite of the European type of relapsing fever, *S. recurrentis*, touches so closely upon the mechanism of infection in the other relapsing fevers that it needs no apology to consider how far the observations I have detailed in connexion with *S. duttoni* fit in with the facts and views our French colleagues have recorded.

Personally, I had long felt it to be a very weak point that little in the way of corroboration of my observations was forthcoming from the voluminous studies which had been made upon the very closely allied organism of European relapsing fever. It was not until Nicolle and his colleagues had, in a series of most valuable communications, established beyond doubt the part played by the louse in the transmission of this fever that real progress could be made in the study of *S. recurrentis*. The work in question is too long to permit of my doing more than giving you, in baldest outline, their main conclusions.

Tracing the fate of spirochætes ingested by lice by means of daily dissections and examination of specimens, both by staining and by dark-ground observation, latterly also by sections of lice stained by the Cajal-Levaditi method, they find that the spirochætes become rapidly immobilized in the stomach, altered in appearance and staining, and disappear altogether after about twenty-four hours. No further trace of them could be found until on or soon after the sixth day, when they suddenly reappeared in great numbers in the body cavity of the louse. These new spirochætes were actively motile, typical in shape, but at first thinner and shorter than those of the blood; later they became identical with the blood forms. Having made their appearance, they may persist up to the twenty-second day. The examination by means of stained sections of lice showed that the original spirochætes are taken into the stomach cells, but they could see no trace of them there later than forty hours after the feed on infected blood. When the young spirochætes, as they too name them, make their appearance in about 148 hours sections show that they are absent from the lumen of the gut and from the biting parts, but abundant in the body cavity and especially in the lacunary spaces in the legs. Testing the infectivity by inoculations of crushed lice at various periods

after the infecting feeds, and employing in these tests not only monkeys but men, they show that (1) up to the fifth day successful infection is inconstant; (2) on the sixth day, in spite of invariable absence of demonstrable spirochætes, infection is constant; (3) after this, infection is again inconstant, and may not result even when the presence of spirochætes is demonstrated.

Their observations lead them to the conclusion that there is an invisible, pre-spirillar stage of the spirochæte in the louse, and that it is during this stage, and at the moment just before the sudden appearance of great numbers of young spirochætes, that the louse is most dangerously infective, although it *may* also prove infective at any time from just after the feed on spirochæte blood up to the fifteenth day. Infection of man they consider takes place through the crushing of lice on the skin or their forcible removal, the fragility of the legs making it easy to imagine how the spirochætes escape and gain entrance to the bite or scratch. Infection through the biting parts of the louse they have shown conclusively does not occur. They consider that the spirochætes of adult form only exceptionally multiply in the louse, by transverse or other mode of fission, since division forms are hardly ever seen; whereas the young forms, when first they are observed, are present in immense numbers, and do not increase further; on the contrary, the larger they grow the fewer are there found and the less pronounced their motility. They consider it probable that a similar train of events happens in man, and Sergent and Foley have shown in this case that the blood may, at a certain stage, be highly virulent in spite of the absence of spirochætes. In general, they consider that the only active form of the spirochæte, whether in man or in the louse, is the "invisible" form which alone is virulent and capable of division.

I shall not attempt a detailed comparison of the various points brought out in this important research with analogous observations in connexion with the behaviour of *S. duttoni* in *O. moubata*, as I think it will be sufficiently clear that there is a very close correspondence in the behaviour of the two spirochætes in their respective arthropod vectors. I confess that I shall be not only disappointed but also surprised if further work does not reveal the "invisible" stage of *S. recurrentis* as a granular stage similar to that which occurs in *S. duttoni*, and probably taking its origin in the terminal or lateral buds of which I have made so frequent mention. The recent observation of Kennedy in Baghdad of such buds in lice taken from relapsing fever cases may perhaps be a further link in the chain of evidence which is lengthening around this difficult subject.

Although it would take me too far from my subject to discuss the significance of the Rickettsia bodies now associated with typhus and trench fevers it should not be forgotten how close a resemblance they bear to these spirochætal granules, and further researches in connexion with them will be eagerly awaited.

Conclusion.

I could wish that the observations which I have laid before you were sufficiently clear in their interpretation to allow of my formulating conclusions of a definite nature, such as might be generally accepted. The time has not yet arrived for that, and further research is clearly necessary. The most that I feel entitled to do is to give a short summary of my personal opinions, for what they are worth, as to the apparent life-history of *S. duttoni*, in the light of my own observations and of my interpretation of those made by others on this and closely allied spirochætes. The following appears to me to be the probable train of events.

Starting from a patient suffering from tick fever, whose blood contains *S. duttoni* and is bitten by a tick, the spirochætes taken into the tick's intestinal tract gradually lose their motility, and many undergo structural changes such as the formation of granules and the extrusion of buds. They do not multiply in the tick in this form and rapidly disappear, few being left by the eighth to tenth day. The granules are either extruded during life or, more probably, are liberated by the breaking down of the spirochætes, either in the gut or within the tissues into which they have wandered. These granules present themselves as small clumps embedded in a homogeneous matrix, and are found chiefly in the cells lining the Malpighian tubules and in the genital tissues. They persist throughout the life of the tick, and are to be found at times in the intra-ovarian eggs as well as in the young nymphs hatched from these eggs. In the young nymph the granules are capable of multiplying, sometimes to an enormous extent. The buds formed on the ingested spirochætes contain similar granules, and when separated from the parent spirochæte are difficult to distinguish from the other granule clumps. They are rare in comparison with the number of granule clumps arising from the segmentation of the chromatin.

Under certain conditions, of which a high temperature is one, though probably not the only one, spirochætes tend to reappear in the tick about ten days after feeding. This occurs suddenly, immense numbers being found in the tissues and cells of the body. These are at first different in appearance to the blood forms, being smaller, thinner, more faintly staining, and showing greater irregularity in their curves, they are actively motile. These young spirochætes have been frequently seen in stained films arising, apparently, from granules, and by the continuous observation of living specimens, at a suitable temperature, this origin has been confirmed. When once young spirochætes have made their appearance, they tend to persist in this form throughout the life of the tick, and there is some reason to think that it is this form, or the granule stage immediately preceding it, which is most infective.

It appears probable that the relapse in man and in animals may be

due to the development of fresh crops of spirochætes out of granules formed by those organisms which caused the first attack.

Observations upon other pathogenic spirochætes make it probable that a similar cycle of development is common to them all.

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UPWARD DISPLACEMENT OF THE DIAPHRAGM, WITH SPECIAL REFERENCE TO THE DIAGNOSIS OF AMŒBIC HEPATITIS.

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In November, 1919, a paper written in 1917 in collaboration with Dr. Janet Walton was published in the JOURNAL OF THE ROYAL ARMY MEDICAL CORPS, in which we described certain physical signs which we believed to be characteristic of amœbic and other forms of hepatitis. Since that paper was written a further experience of two years in charge of medical divisions in Salonika has afforded substantial evidence of the value of these signs, and also enabled me to correct that description in some of its details. The cardinal signs there described were: (1) Raised liver dullness (deep); (2) displacement of the heart upwards and to the left; (3) certain areas of impairment in the lungs, especially of the right apex. I have now notes of ninety-four additional cases presenting these signs in which it was possible to reach a definite conclusion as to the condition causing them. In eighteen of these there was direct evidence of upward displacement of the right side of the diaphragm; in sixty-four more there was evidence of amœbic infection, associated in most cases with symptoms of hepatitis; in one of these—a cyst carrier—a swollen and discoloured liver was seen at laparotomy. The cases were as follows:—

X-ray evidence of displacement of the diaphragm	12
Liver abscess found	4
Subphrenic abscess	2
Secondary malignant growth in liver	1
Entamœba histolytica or *E. histolytica* cysts found	31
"Amœbæ" present	2
Ulcers of large intestine found post mortem	1
Definite effect of emetine on signs and symptoms	30
	83

Of the eleven remaining cases four had conditions which I recognize in the light of later experience as causes of displacement of the diaphragm other than hepatic, while in seven the signs were apparently caused by pulmonary conditions, and they must be classed as errors. It is one of the objects of this paper to show how such errors may be avoided. The classification in the above table is exclusive, i.e., although cysts were found in some of the X-ray and liver abscess cases, and some of the abscesses were X-rayed, each patient is included under one heading only.

(1) The clinical value of these signs is conclusively shown by the fact

that in the spring of 1918, when amœbiasis was generally regarded as a very uncommon condition in Salonika, thirty-eight definite cases were found in a few weeks in one hospital, of which twenty-four were recognized by the hepatic signs alone. In thirty-one of these the organism was demonstrated by Captain Richards, who, in view of the unexpected number of positive results, took the precaution of asking the British Museum delegate, Mr. Ramsbotham, to confirm his findings. In the other seven there was an unmistakeable response to emetine. About twice this number were seen but were not completely worked out. The disease was thus shown to be comparatively common. In April Major E. P. Gunson kindly undertook to test the value of the signs as a guide to the presence of amœbiasis, and after five months' investigation informed me that he had been able to confirm most of my findings and had found amœbiasis quite common among the troops. Another officer, Captain Scott, in charge of bacillary dysentery wards, told me that by means of these signs he had been able to pick out a very large proportion of amœbic cases among them, *Entamœba histolytica* being demonstrated in the great majority of those selected.

(2) In our earlier paper we expressed the opinion that the displacement of the diaphragm in amœbic hepatitis could not be the result of mechanical pressure. The following case establishes this view and leads to a wider generalization.

Patient was admitted on March 5, 1918, with well-marked physical signs suggesting liver abscess. The deep liver dullness rose to the middle of the fourth rib, absolute dullness began at the fifth rib. The apex beat was in the fourth space, three centimetres outside the nipple line. There was marked impairment above the right clavicle and from the middle of the third right space downward. Behind, the whole right side was somewhat higher pitched to percussion than the left, the right upper lobe was much impaired, and there was a patch of almost absolute dullness opposite the sixth and seventh spines on the right side. The deep liver dullness began just below the level of the seventh spine, and the lung resonance began to shade off opposite the ninth spine, ending just below the tenth. Vocal vibrations were present over the whole of both sides and were much increased over the front of the right upper lobe. There were no signs of fluid. The breath sounds were relatively weak at the right base and were very weak over the dull patch behind. In full inspiration the left lung behind reached about an inch lower than the right. There were high fever and sweating and tenderness in the right lumbar region. After four doses of emetine in forty-eight hours there was no change, and the leucocyte count was 29,000 with eighty-four per cent of polymorphs. At operation by Major Gauntlett a small perinephric abscess containing three or four drachms of pus was found at the upper pole of the right kidney in contact with the posterior edge of the diaphragm. The patient made a complete

recovery without any sign of intrathoracic disease, and there was no past history pointing to lung trouble.

It appears, then, that any area of inflammation in direct contact with the diaphragm causes a reflex dilatation of that leaf of the diaphragm with which it is in contact; and this seems to be true whether the inflammation is in contact with the under or upper surface. (It is possible that other intra-abdominal conditions remote from the diaphragm may produce the same effect, but in two cases of appendicitis seen presenting the signs of phrenic displacement the onset had been with acute diarrhœa, and one of the patients had spent a year in Egypt; another similar case of appendicitis had acute dysentery at the same time, the whole condition clearing up in forty-eight hours on emetine without operation.)

This generalization immediately led to the recognition of an analogous, and almost equally important, condition on the left side, due to perisplenitis of which malaria was by far the commonest cause.

(3) The full clinical picture presents five stages which may co-exist in any combination, the first being invariably present except during remissions of acute hepatitis. These stages are:—

(i) Dilatation of the diaphragm.
(ii) Stasis of the diaphragm.
(iii) Distension of the diaphragm.
(iv) Ascending inflammation of intrathoracic organs.
(v) Descending infection of the lungs.

(i) Dilatation of the diaphragm is analogous to dilatation of a cardiac ventricle, and is very common in cyst carriers. With the orthodiagraph the diaphragm may be seen to be moving quite freely, but rising with each expiration to the fourth rib instead of the fifth as in the normal chest. The excursion during quiet breathing does not appear to be increased; the movement is normal, but takes place at an abnormally high level. This can only be demonstrated on the right side; the existence of a similar condition on the left side is an inference from the associated heart and lung changes.

(ii) Stasis of the diaphragm accompanies more acute inflammations; the diaphragm moves badly or remains stationary at the level of the fourth rib. Stasis occurs whenever there is restricted movement of the abdomen from whatever cause, as has been shown by Dr. Charlton Briscoe after operations on the intestines, but not necessarily at a high level.

(iii) Distension is a mechanical effect of fore and aft enlargement of the liver.

(iv) Ascending inflammation produces pleurisy or pericarditis with or without effusion. A small pleural effusion is common in the neighbourhood of an advancing abscess and is very suggestive of suppuration; dry pleurisy has not the same significance and is often met with above a malarial spleen.

(v) Descending infection produces bronchitis or broncho-pneumonia; when combined with ascending inflammation of the pleura, a pleural abscess may result.

(4) In the light of later observations a more precise account of the clinical signs is needed; right-sided conditions only will be considered here.

(i) *Impairment reaching to the Fourth Rib.*—While this is essential to the diagnosis, there are unfortunately a number of intrathoracic conditions which can produce this sign, one of the most important being that condition which is associated with dense root-shadows in the radiogram. Examination with the orthodiagraph will decide the diagnosis at once, but this is so often impracticable that distinction by clinical methods is of importance. When the orthodiagraph is available, care must be taken to allow time for emotional disturbance to pass off. Examinations with the patient lying on his face are liable to various errors due to mechanical interference with abdominal breathing. If the orthodiagraph is not used, the exact level at which impairment begins should be carefully determined in the position of expiration during quiet normal breathing. This should be repeated at the end of the physical examination, when the patient has become accustomed to being handled. The level taken is that at which there is an abrupt change in the pitch of the note produced by moderate percussion. An X-ray study of forty-six cases and a few post-mortem experiments have shown that unless there is some gross lesion, such as empyema, there is always a definite line at which the pitch rises sharply corresponding to the position of the upper surface of the diaphragm. This line is quite easy to make out in front, and can be found behind too, but with less precision. If, therefore, there is no such line at or above the level of the middle of the fourth rib in the nipple line (or just internal to it), any impairment present in the fourth space should not be regarded as evidence of hepatitis. On the other hand, the change corresponding to the level of the diaphragm is rarely, if ever, higher than the upper border of the fourth rib. Areas of impairment beginning at a higher level than this are commonly associated with dilatation of the diaphragm but are due to lung changes. If the change of note is found within these limits, it is absolutely necessary to look for confirmatory signs in the heart and lungs before deciding that it is caused by a raised diaphragm.

(ii) *The Heart Sign.*—The essential feature of this sign is that the maximum cardiac pulsation should be felt in the fourth left space outside the nipple line, or at least not more than one centimetre internal to it, and that the apex beat should not be felt in the fifth space. The pulsation should be localized and not diffuse. Marked pulsation may be present in the third space, and the apex may be just felt at the lower border of the fifth rib. The observation is made in the position of expiration and the sign is present, and may be more easily made out, when the patient is standing. In the better marked cases the apex beat is in the fourth space outside the nipple line. Apart from easily recognized heart lesions this sign has almost invariably been found associated with displacement of one or other leaf of the diaphragm. I believe it to be due to forward rotation of the heart bringing the left ventricle into contact with the fourth space

followed by displacement upward and to the left. It must be carefully distinguished from a much commoner condition in which the right ventricle is felt beating in the fourth space two or more centimetres internal to the nipple line. This is usually associated with some chronic pulmonary lesion and is a more diffuse impulse, and the apex beat is usually to be found in the fifth space. When phrenic displacement is present the left border of the heart is found by percussion in or external to the nipple line, and the upper border at the upper border of the third rib or even higher. If no pulsation can be felt, the apex beat may be heard in the situation indicated. This displacement of the heart may be seen with the orthodiagraph. (In two cases of left lobe liver abscess the maximum pulsation has been found in the fourth space about two centimetres internal to the nipple line. In both cases the whole heart was displaced to the right and the apex beat was heard in the fourth space some way internal to the nipple.)

(iii) *The Lung Changes.*—These will be best understood by reference to the charts. In simple dilatation the whole lung on the affected side is relaxed, and this relaxation produces a slightly higher pitch in the percussion note—an incipient Skodaic note—which is most marked in the shaded parts, viz., at the apex of the upper lobe in front and behind, and over a band about four centimetres wide opposite the fourth and fifth spines. The lung is shortened and the sharp edge of the lung resonance is blurred. There is also a triangle of "sharpened" note at the inner end of the third right space. In the more marked cases, and especially when there is stasis, high-pitched resonance gives way to distinct impairment or even dullness, and the areas spread, so that the whole third space may be much impaired and give the impression that the liver is reaching to the third rib. With stasis the breath sounds become weak, and as the relaxed patches become de-aerated there may be bronchial breathing. Later these patches especially at the bases, may become infected, and secondary broncho-pneumonia result. In these stages, and indeed in every stage, the lung signs are often the most obvious feature and may very easily lead to mistakes in diagnosis.

The differential diagnosis between right and left-sided phrenic dilatation and right-sided fibrosis of the lung is shown in the charts. The most important distinguishing points are the position of the heart and the relative impairment over the second rib in front. In right-sided fibrosis the heart is commonly displaced to the right, in dilatation of either leaf of the diaphragm it moves upwards and to the left. This displacement causes relaxation of the lower part of the left upper lobe in front with sharpened note while the corresponding area on the right side is clear; in right-sided fibrosis there is usually some impairment below the right clavicle as well as above, while the left side is clear. Left-sided fibrosis with pleural thickening may closely simulate left-sided phrenic dilatation; but the contraction and diminished expansion of the left chest will usually suffice to distinguish it. (In left lobe liver abscess the lung signs are chiefly on the left, but to some extent bilateral.)

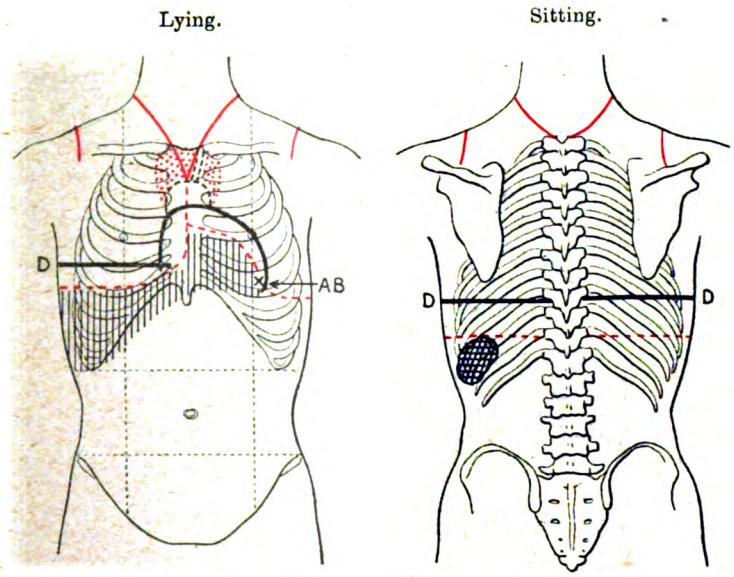
It will be seen that early bilateral tubercle, tubercular glands, or right-sided fibrosis combined with malarial splenitis may produce pictures very much like these, for in all these conditions, as in phrenic dilatation, there is usually a change of note at both the fourth and the fifth ribs, and it is often very difficult indeed to decide which of these levels corresponds to the diaphragm. A method, which so far, in a series of twenty-five cases, has given consistent results may be of use. It depends on the fact that when the right arm is raised above the head the costo-diaphragmatic sulcus is opened and the lung slips down into it without displacement of the diaphragm. It is a method of separating costal from diaphragmatic inspiration. The levels are first marked out with great care and the distance between the levels of impairment in the neighbourhood of the fourth and fifth ribs is measured. The arm is then raised to just beyond a right angle with the hand behind the head, and these levels are again determined and measured. If the diaphragm is at the upper level the second measurement will be definitely larger than the first; if it is at the lower level it will be smaller. In six out of eleven positive cases the diaphragm was seen to be raised with the orthodiagraph, four were definite cases of amœbic hepatitis, and the remaining case had marked displacement of the heart; in seven out of fourteen negative cases X-ray examination confirmed the position of the diaphragm at the lower level, and the rest were proved cases of tuberculosis, enterica, early pneumonia or pleural abscess. This sign may give ambiguous results, particularly when adhesions are present, and of course it will not distinguish between the diaphragm and structures adherent to its upper surface.

Distension of the diaphragm may obliterate the costo-diaphragmatic sulcus, producing marked shortening of the lung and even loss of tidal resonance. This is usually the case when an abscess is bulging towards the chest-wall, but is not diagnostic of suppuration though very suggestive of it.

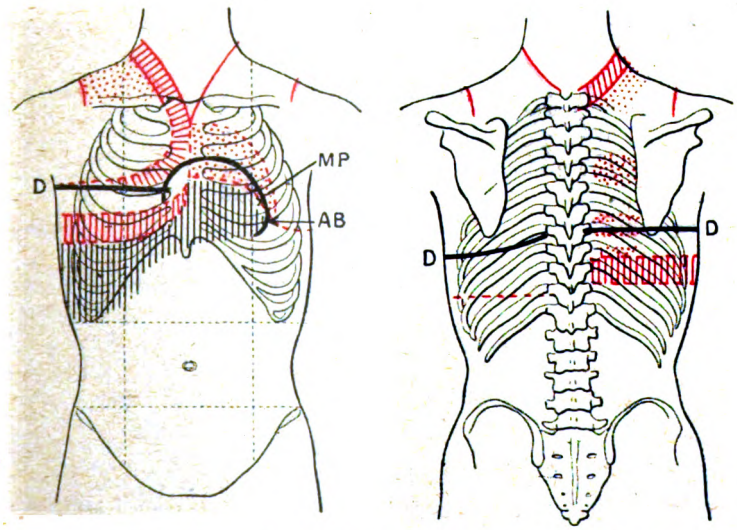
Weak breath sounds and signs of consolidation denote stasis; a common finding is a broad band of bronchial breathing extending right across the back and reaching to about the eighth spine from the base, but occasionally the upper lobe is affected more than the base. A similar left basal condition was pointed out by Lieutenant-Colonel A. W. Falconer in malaria and ascribed by him to collapse due to plugging of a bronchus.

When diaphragmatic pleurisy results from ascending inflammation the diagnosis must depend on other evidences of hepatitis, because this condition by itself seems to be able to cause reflex displacement of the diaphragm, but it may be said that in an amœbic centre hepatic inflammation, and particularly abscess, is a very common cause of right basal pleurisy and pleural abscess.

The difficulty is not so great when descending infection is present for, in the absence of associated diaphragmatic pleurisy or of mechanical

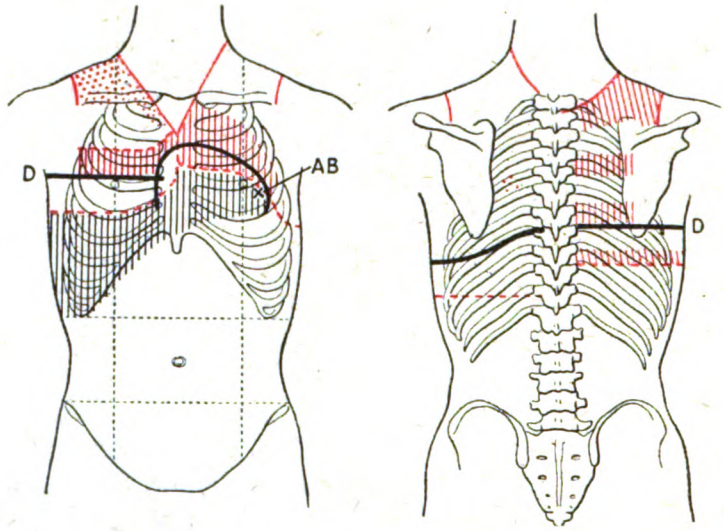


CHEST CHART 1.—Normal chest.

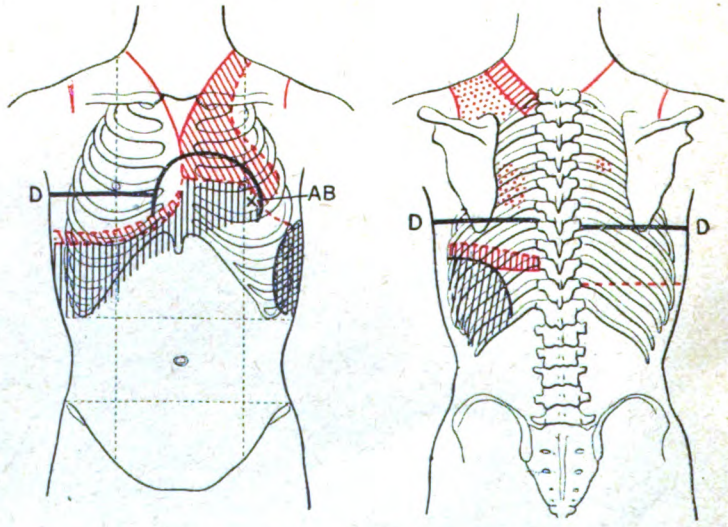


CHEST CHART 2.—Moderate right-sided phrenic dilatation.

D = Diaphragm. AB = Apex beat. MP = Maximum pulsation. /// = Impairment.
: : : = Slight impairment or "sharpening." Red line = Edge of lung.



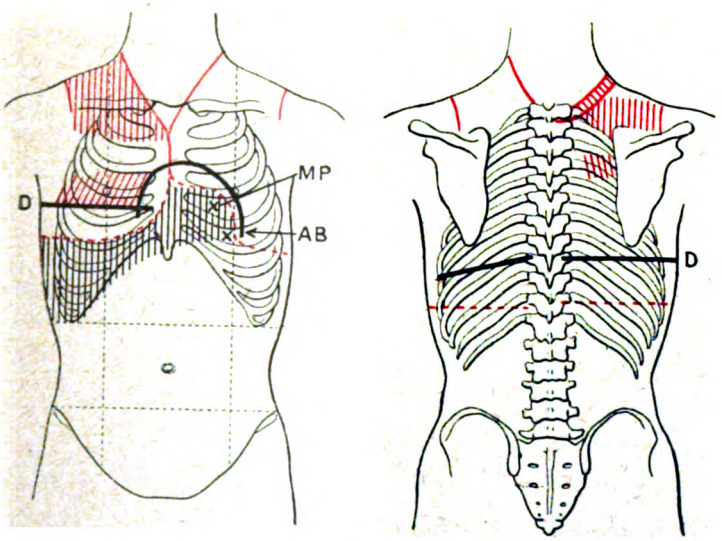
CHEST CHART 3.—Marked right-sided phrenic dilatation.



CHEST CHART 4.—Left-sided phrenic dilatation.

D = Diaphragm. AB = Apex beat. /// = Impairment.
Red line = Edge of lung.

displacement by adhesions or contractions, broncho-pneumonia itself does not raise the diaphragm—at least to the extent met with in hepatitis. The clinical picture now is that of right basal broncho-pneumonia together with displacement of heart and diaphragm and collateral evidence of hepatitis and amœbiasis. If the amœbic element underlying the condition is overlooked, it may progress to a fatal issue, but if emetine is given there is usually a marked improvement within forty-eight hours, the further course depending on the extent and virulence of the secondary infection. The charts show the effect of emetine in these cases.



CHEST CHART 5.—Right-sided fibrosis of lung.

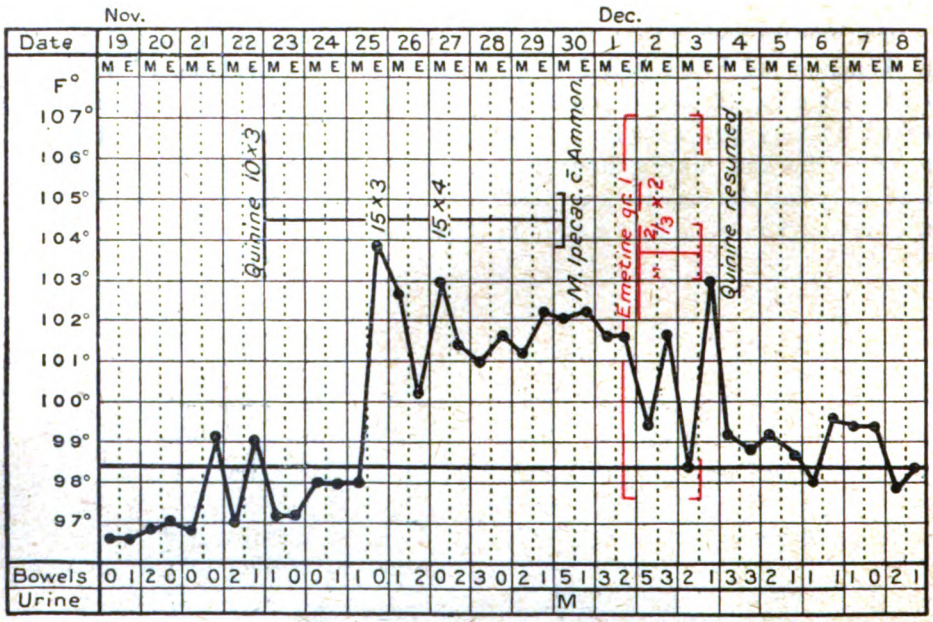
D = Diaphragm. AB = Apex beat. MP = Maximum pulsation. /// = Impairment.
Red line = Edge of lung.

Chart 1 is from a case of acute hepatitis with bronchitis; forty-eight hours' emetine treatment cleared it up.

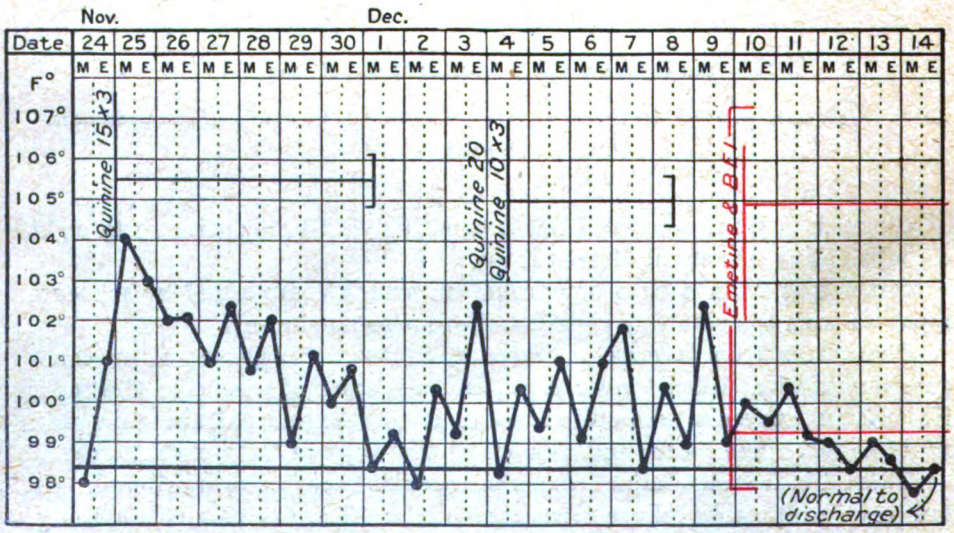
Chart 2 is from a case of chronic bronchitis complicated by subacute hepatitis with the resulting right basal broncho-pneumonia.

Chart 3 is from a case of severe "influenzal" right basal broncho-pneumonia with definite liver signs and a history of service in Gallipoli. He was in extremis when the treatment was begun; within thirty-six hours he felt much better and was out of the wood in forty-eight hours.

Chart 4 is from a similar case, who was also reported as moribund. He had very well-marked liver signs and bilateral basal bronchial breathing. In this case also subjective improvement took place within twenty-four hours.

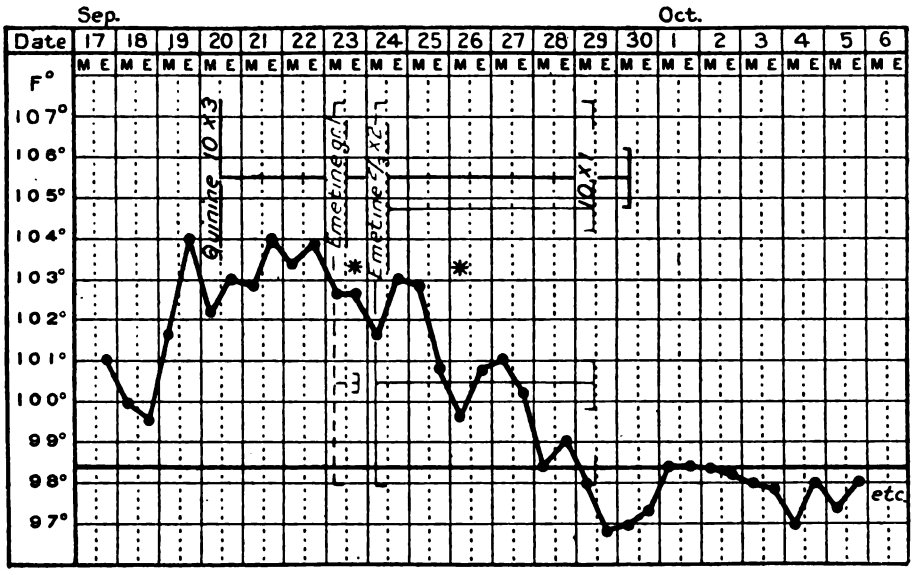


TEMPERATURE CHART 1.—Pte. F.

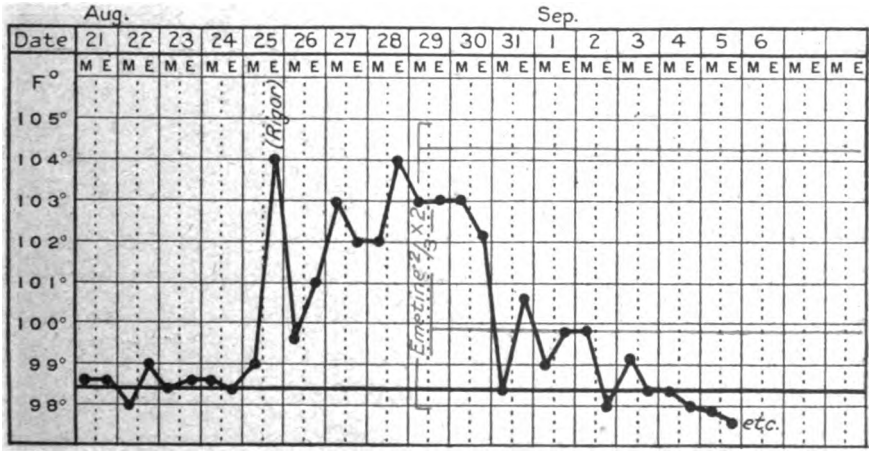


TEMPERATURE CHART 2.—Lt. H.

Chart 5 is from a patient who had just had his appendix removed. He developed right basal broncho-pneumonia shortly after, and it was thought to be due to the operation. On examination on the fifth day well-marked



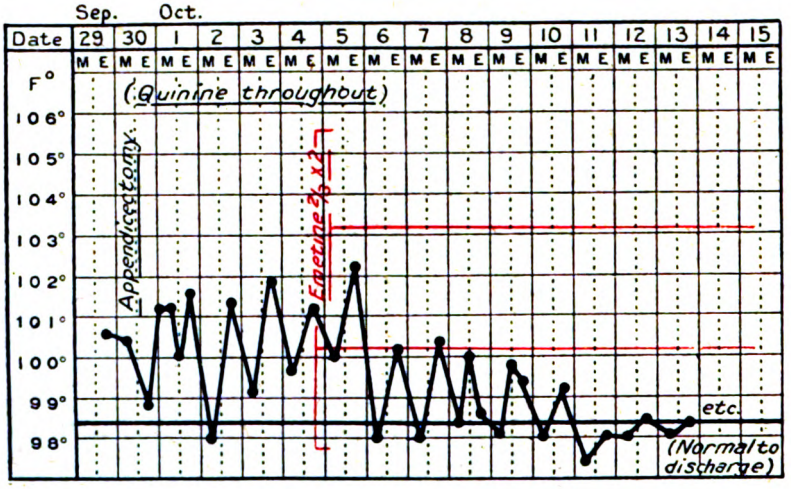
TEMPERATURE CHART 3.—Gr. M.



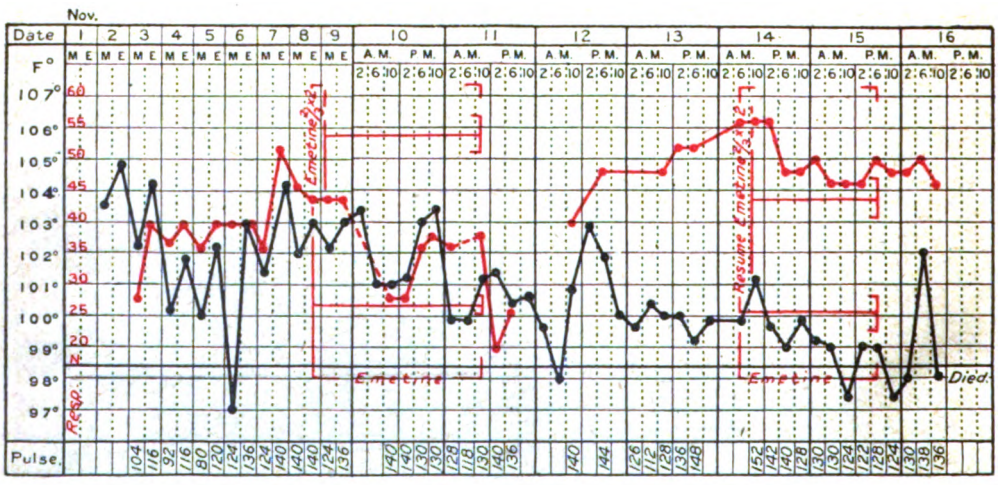
TEMPERATURE CHART 4.—Br. M.

bronchial breathing was heard at both bases and there were characteristic liver signs. I did not at that time know that Dr. Briscoe had described basal collapse as a common sequel of abdominal operations and the predisposing cause of post-operative broncho-pneumonia, and consequently

felt confident that this was a case of amœbic typhlo-appendicitis and hepatitis. Though recognizing now that the grounds for this confidence were insufficient, I think the reaction to emetine as shown in the chart is definitely specific. It is clear that after the third dose the pulmonary con-



TEMPERATURE CHART 5.—Pte. G.



TEMPERATURE CHART 6.—Dr. S.

dition goes on its normal course but at a much lower level in consequence of the removal of a contributory factor. It may be noted also that the respirations were recorded as 32 before the operation.

Chart 6 suggests very strongly that the timely use of emetine in these

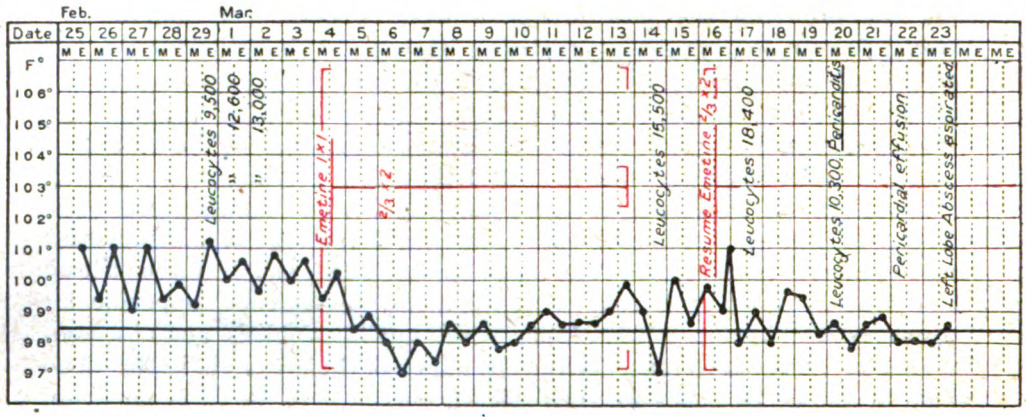
cases may avert death. A fatal relapse followed the premature cessation of treatment. In an exactly similar case in which emetine was not given, the large intestine was found studded with small ulcers at autopsy. In yet another untreated case the pathologist reported acute hepatitis.

(An analogous and equally important left basal broncho-pneumonia is common in chronic malaria. It has seemed that preventive treatment in cases of influenza in malarial subjects, by energetic measures directed to controlling the malaria, removing the splenic congestion, expanding the lung (by propping the patient up), and disinfecting the mouth and throat, has in many cases averted a threatened infection of the left base when fine crepitations or even bronchial breathing have already appeared.)

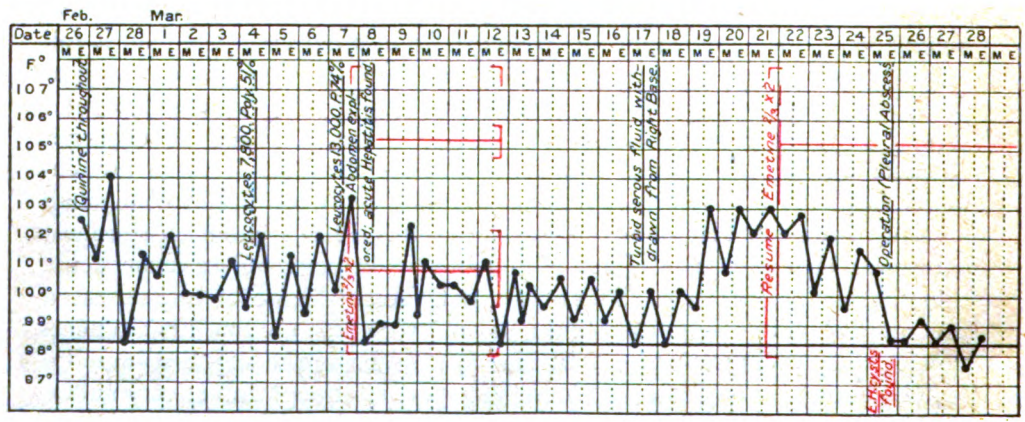
(5) The signs described are by no means diagnostic of hepatitis; it is possible (and even a priori probable) that they may be present in any condition associated with tenderness and rigidity of the abdomen. As already mentioned, they have been present in four cases of appendicitis; but in none of these could amœbiasis be excluded, and in three at least there was evidence in favour of it. In my experience, appendicular symptoms are common in association with amœbic typhlitis, and abscesses may be formed by perforation of the cæcum or of the appendix itself. The value of these signs lies in their significance where there is no acute abdominal tenderness. In acute hepatitis there is no great difficulty in recognizing what is the matter, but in the chronic form the symptoms do not as a rule at first sight seem to point to the liver. The commonest complaint is of "lumbago" or "kidneys"; in other cases the pain is felt in the epigastrium, or not uncommonly is referred to some part of the right shoulder. In yet other cases the patient complains of cough or irregular fever. Physical examination of the abdomen and liver may be negative. In chronic hepatitis, or even in chronic abscess, the liver is often not enlarged downwards, tenderness is slight and is usually localized to one small area in the epigastrium or at the costal margin. Measurement of the chest shows no enlargement and no diminished movement unless some acute inflammation is present. There is usually some degree of resistance on pressing below the right costal margin, and very commonly a little tenderness on deep pressure in the right iliac fossa. Even the slightest jaundice is not common in any form of amœbic hepatitis, though infective jaundice may predispose to the development of liver abscess in a carrier. When therefore these signs are found associated with slight, chronic and indefinite pains in the region of the lower ribs or the right shoulder, in front or behind, with perhaps irregular fever or occasional rigors, and when neither diaphragmatic pleurisy nor acute tenderness of the abdomen can be found, the question of chronic hepatitis arises, and with it the cognate question of chronic amœbic infection.

(6) The diagnosis of amœbiasis is most readily made by observing the effect of a trial course of emetine, two-thirds of a grain twice a day. There

is usually subjective improvement in twenty-four hours, objective general improvement within forty-eight hours, and total disappearance of symptoms by the fourth day. The signs also usually disappear in a few days, but in long-standing cases adhesions may cause a permanent displacement of diaphragm and heart In the absence of intercurrent disease or of obvious secondary infections, such as broncho-pneumonia, an incomplete reaction to emetine is a valuable evidence of the existence of a pleural or hepatic abscess.



TEMPERATURE CHART 7.— Pte. H. Abscess at back of left lobe of liver.



TEMPERATURE CHART 8.—Pte. E. F. Acute hepatitis seen at first (exploratory) operation; pleural abscess found at second operation. *Entamœba histolytica* cysts found for the first time on the day of the second operation.

While laboratory confirmation is always desirable, it is now well recognized that only repeated and prolonged examinations of absolutely fresh stools by an expert protozoologist can exclude amœbiasis, and this is by no means often available. But even when it is, there appears to be a definite seasonal cycle in the laboratory findings, corresponding to a

similar cycle in the clinical manifestations. Thus during three and a half years in Malta and Salonika chronic hepatitis and reports of the presence of cysts were common in winter and early spring, while in summer chronic or intermittent diarrhœa with negative findings was the usual clinical picture. In these cases the number of positive reports was materially increased by taking special precautions to have the stool examined within a few minutes of being passed, and by giving saline purges a few hours before; but though amœbæ were found by this means in several previously negative cases, the report was usually qualified by the addition, "species indeterminate." In the early summer subacute hepatitis and acute diarrhœa were associated with reports of *Entamœba histolytica*, sometimes with cysts as well; while in the autumn acute hepatitis and amœbic dysentery were at their maximum. The following cases illustrate this cycle.

(i) A sister, suspected of chronic appendicitis, was found in February, 1918, to have well-marked hepatic signs, and numerous cysts were found at first examination. Emetine one grain every morning and BEI two grains every evening for ten days had no effect on the cysts. A full nine-day course of emetine and diminishing doses of ipecac., beginning with forty-five grains, was equally useless. This was followed by three days of the Panama bismuth-milk treatment, also without success. Treatment was then abandoned. Two more positive results were obtained at weekly intervals, and then the passage of cysts ceased spontaneously.

(ii) Patient admitted in October with chronic diarrhœa with blood. No amœbæ were found, but the diarrhœa yielded at once to emetine. In November, during convalescence, cysts were found. They were passed continuously in spite of several variants of emetine treatment till March, when seven consecutive negative results were obtained. In May he was readmitted with diarrhœa as before. No amœbæ were found, but again the diarrhœa cleared up at once on emetine.

(iii) Patient admitted in November with hepatic syndrome and recent history of dysentery, no organism having been found. Cysts were found at the second examination. This patient also continued to pass cysts all the winter in spite of all treatment, and was released in April after seven consecutive negative results.

All these three cases were examined under ideal laboratory conditions, and the results show clearly that reliance on a negative report may be seriously misleading. A still more dangerous source of error is the frequent co-existence of infection with bacilli of the Flexner group. Thus, out of 33 cases with history of dysentery or severe diarrhœa in whom cysts were found, Flexner had been reported during the dysenteric attack in 8 and Shiga in 1. One of the Flexner cases developed a double liver abscess shortly after the Flexner dysentery; cysts were not found till after the second abscess had been opened. Many of these Flexner

bacilli are found on more detailed examination to be atypical. In 210 Peninsula patients, mostly convalescent from dysentery, Flexner group bacilli were found by the writer in about five per cent. Agglutinable bacilli of this group were isolated from eleven cases, but only three (two Flexners and a "Y") conformed to standard on prolonged culture. The "Y," curiously enough, was from a patient who had never had dysentery or diarrhœa.

These facts show that the lack of laboratory confirmation should not be allowed to weigh against strong clinical suspicion or be regarded as a contra-indication to emetine treatment. In the urgent cases in which emetine may be of crucial importance there is no time to wait for confirmation. The patient from whom Chart 8 was taken was unquestionably saved by the resumption of emetine on March 21, though repeated examinations had up to that time been negative, and cysts were not found till March 25.

The relation between infection and intestinal symptoms is shown by the following figures. Out of 36 patients with hepatic signs in whom the organism or a liver abscess was found, 15 had had dysentery (diagnosed as Flexner in 2), 8 had had recurrent diarrhœa (4 slight only), 3 had had diarrhœa twice (2 slight), 3 had had single attacks of diarrhœa and 5 none at all. The proportion with history of dysentery is doubtless much too high, as cases were at first specially sought in dysentery wards. Taking only those seen in 1918, the number of dysentery histories is 10 out of 33; severe diarrhœa 4; occasional, slight or single attacks 11, and none 5. A far more important item in the history is exposure to infection by residence in an endemic area. Till the autumn of 1917 practically all the cases were from Gallipoli or Egypt, or close contact with men from these areas was to be traced; while out of the 39 cases seen in 1918 in whom the source of infection was sought, 13 were from Gallipoli, Egypt, India or China, 2 were close contacts of Gallipoli men, and 4 had nursed amœbic dysentery or liver abscess; so that even then nearly half the amœbiasis in Macedonia was directly traceable to an endemic centre. Conversely, clinical signs of hepatitis were so common among Egypt and Peninsula men, and so much commoner in them than a history of dysentery, common as that was, as to suggest very strongly that the majority of the men who went to these stations became infected, with or without intestinal symptoms, and that a very large proportion of them continued to harbour the amœba indefinitely.

(7) The problem of treatment is the problem of the cyst-carrier, but the symptoms may often be temporarily relieved by saline purgation. Constipation and "chill" are the chief predisposing factors, and both signs and symptoms often disappear after purgation, spontaneous or medicinal, particularly in the acute cases. If the view that infection and re-infection are practically inevitable while living in an endemic centre be established, this measure will often be all that is needed, and the

attempt at eradication may be postponed till the patient leaves the amœbic area; if it fails, a few doses of emetine will give relief. But in acute cases, and particularly when intrathoracic complications are threatening, the use of emetine is imperative, and that without waiting for laboratory confirmation. The danger of delay is far greater than the (mainly hypothetical) risk to the heart from its depressant action, which with simple precautions and careful watching is negligible. I have never in eight years' experience had cause to regret trying it even when it has done no good, though I have several times had to regret its omission.

My thanks are due to many medical officers and particularly to the pathologist, Captain Richards, R.A.M.C.T., and to Major H. G. Frean, radiologist to the hospital; also to my surgical colleague, Lieutenant-Colonel E. G. Gauntlett, R.A.M.C.T., C.B.E., D.S.O.; and to Lieutenant-Colonel P. Mitchell, R.A.M.C.T., C.B.E., commanding one of the hospitals, for unfailing interest and encouragement in the clinical work of the division.

Summary and Conclusions.

(1) Inflammation in immediate contact with any part of the diaphragm causes a reflex dilatation of that leaf of the diaphragm with which it is in contact.

(2) This condition may be recognized by means of the signs described.

(3) It predisposes to serious intrathoracic infections, which may be greatly benefited by treatment of the underlying cause.

(4) In endemic centres amœbiasis and malaria are the commonest causes of right- and left-sided dilatation respectively.

(5) Under suitable climatic conditions the prevalence of these signs (on the right side) is a valuable index of the prevalence of amœbic infection in the community.

(6) Amœbiasis would seem to be a great deal commoner in endemic centres than either the prevalence of dysentery or the results of laboratory investigation would indicate.

THE OCCURRENCE OF A MULTIPLE SEPTICÆMIA IN MICE DUE TO *BACILLUS INFLUENZÆ*, *PNEUMOCOCCUS* AND *MICROCOCCUS CATARRHALIS*, FOLLOWING THE INOCULATION OF SPUTUM.

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In discussing the isolation of pneumococci from sputum by mouse inoculation, Avery, Chickering, Cole and Dochez [1] have made the following observations in a monograph on acute lobar pneumonia.

The intraperitoneal inoculation of a mouse with 0·5 to 1 cubic centimetre of an emulsion of sputum from a case of lobar pneumonia is followed by a rapid growth of the pneumococcus in the peritoneal cavity, whilst the greater number of the other organisms present are killed off. Friedländer's bacillus, *Bacillus influenzæ*, and in some cases *Micrococcus catarrhalis*, appear to be more resistant and survive.

The ensuing invasion of the blood-stream by the *Pneumococcus* is accompanied by a *B. influenzæ* septicæmia, if this latter organism is present in the sputum. On the other hand, *M. catarrhalis* and Friedländer's bacillus do not become generalized. Wolf [2] has also reported the occurrence of a double septicæmia in mice and guinea-pigs, produced by inoculation of fresh sputum containing *pneumococci* and *B. influenzæ*, or by the inoculation of mixed cultures of these organisms.

The extensive English literature dealing with the experimental bacteriology of influenza does not, so far as we are aware, contain any reference to this dual invasion of the blood-stream of an animal following subcutaneous inoculation of sputum derived from a case of clinical influenza. That this may be of not uncommon occurrence appears to be evident from the results of a bacteriological investigation made in a case of influenzal broncho-pneumonia. The accompanying brief clinical and bacteriological notes of the case may be of interest in this connexion.

Clinical Notes.

The patient, a laboratory assistant at the Royal Army Medical College, was admitted to hospital with a high temperature of obscure origin unaccompanied by any localizing symptoms. He stated that for seven or eight days before admission he had not been feeling well, and that two

days before the onset of his first symptoms he had been in contact with a case of acute catarrhal coryza. During the first six days he was under observation, his temperature fluctuated between 102° and 104° F. He suffered from a slight cough accompanied by a scanty muco-purulent sputum, but no definite physical signs of pulmonary involvement were apparent. His appearance was suggestive of a profound toxæmia and was accompanied by anorexia and constipation. On the seventh day of observation his temperature was 101° F., falling to normal by the tenth day. Throughout this period the cough became more pronounced, coincidentally the sputum became more copious and more purulent in character. Convalescence was slow, being retarded by bronchitis with a troublesome cough. A chart indicating the course of the temperature is shown in fig. 1.

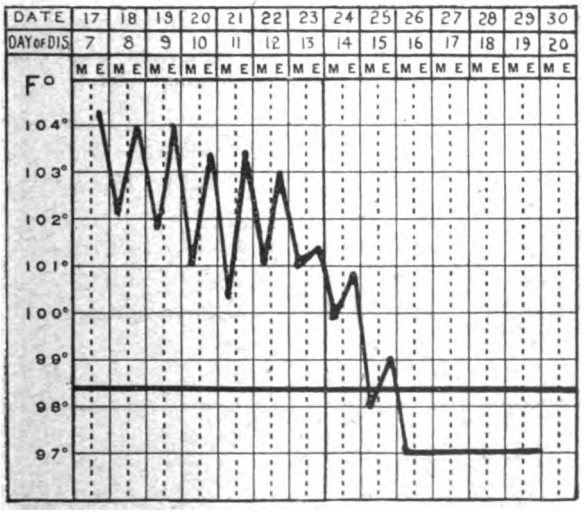

FIG. 1.

BACTERIOLOGICAL INVESTIGATION.

Blood culture at the height of the pyrexia yielded negative results. Direct examination of blood films showed no malarial parasites, whilst a differential count of the leucocytes revealed a slight increase of the polymorphonuclear cells. The possibility of an enteric group infection was excluded by serological tests and by culture of the stools and urine. Similarly, on account of the nature of the patient's employment, a laboratory infection with *Micrococcus melitensis* was considered and excluded. Repeated examinations of the sputum revealed no tubercle bacilli, but a Gram-positive capsulated diplococcus morphologically resembling the *Pneumococcus* was consistently present. *B. influenzæ* was not evident on microscopic examination.

Animal Experiments.

A mouse was inoculated subcutaneously with 0·25 cubic centimetre of a suspension of the sputum in sterile broth. The animal died within twenty-four hours, and was examined within two hours of death. A direct examination of films of the heart-blood, stained by Gram's method, showed numerous Gram-positive capsulated diplococci, and, in addition, a slender Gram-negative bacillus in fewer numbers. Cultures were made with aseptic precautions from the heart-blood on blood agar plates. Three separate types of colonies were evident after incubation for twenty-four hours at 37° C.

These colonies were on examination capable of grouping as follows :—

(*a*) Small, transparent, non-hæmolytic colonies.

(*b*) Smaller than the above, but tending to be confluent.

(*c*) Discrete circular discs with an opaque centre.

Detailed investigation of these three colonies was then undertaken. *Colonies A* consisted of Gram-positive diplococci which had the following properties : They were capsulated, non-hæmolytic, and were soluble in ox bile. They fermented saccharose, lactose, raffinose and inulin. Serologically they could be classified with *Pneumococcus* Type 2. (Rockefeller.)

Table I tabulates the result of agglutination tests carried out with this organism, employing diagnostic type anti-sera which had been prepared from the original Rockefeller Institute strains of *Pneumococcus*.

TABLE I.

Organism	Serum dilutions							Serum
	1/2	1/24	1/48	1/96	1/192	1/384	C.	
Diplococcus from Colonies A	+	−	−	−	−	−	−	Pneumo. Type 1
	++	++	+	+	+	−	−	,, ,, 2
	++	+	−	−	−	−	−	,, ,, 3
	−	−	−	−	−	−	−	Normal serum
Controls of known type Pneumococci against homologous sera								
Pneumococcus—								
Type 1	++	++	+	+	−	−	−	Pneumo. Type 1
Type 2	++	++	++	++	+	+	−	,, ,, 2
Type 3	++	++	++	++	++	+	−	,, ,, 3

Colonies B consisted of minute slender Gram-negative bacilli morphologically identical with *B. influenzæ*. Subculture brought into evidence the hæmophilic character of these organisms. They grew luxuriantly on all media containing blood, but failed to grow on ordinary nutrient agar. In attempting to obtain serological evidence of the identity of the organism under investigation with *B. influenzæ* it was necessary to take into account

the varied antigenic properties of different strains of the latter organism, which recent research on this subject has indicated. Sera had, therefore, to be prepared by immunizing rabbits with a series of authenticated strains of *B. influenzæ* which were available, and it was necessary to test the agglutinating properties of these sera on the organism which had been isolated.

The result of these tests is shown in Table II.

TABLE II.

Organism	Serum dilutions							Serum
	1/12	1/24	1/48	1/96	1/192	1/384	C.	
Bacillus from Colonies B.	++	++	+	−	−	−	−	Fleming
	++	++	++	++	+	−	−	B.S. 4
	+	+	−	−	−	−	−	Lister 1
	+	+	−	−	−	−	−	Lister 2
	+	−	−	−	−	−	−	Lister 3
	−	−	−	−	−	−	−	Griffiths
	−	−	−	−	−	−	−	Normal S.
Controls of known type of *B. influenzæ* against homologous sera.								
Fleming	++	++	++	++	+	−	−	Fleming
B.S. 4	++	++	++	++	+	−	−	B.S. 4

The results of this investigation established the serological identity of the organism with a strain of *B. influenzæ* isolated by Bassett-Smith (B.S.4).

Colonies C.—These more opaque colonies were found to consist of a Gram-negative coccus of small size. Subcultivation showed they grew best on pea extract trypagar; growth also occurring on ordinary nutrient agar, but to a lesser degree. The coccus produced fermentation in no carbohydrate media. From these properties, and from the additional fact that no agglutination was demonstrable with *Meningococcus* diagnostic sera, this organism conformed in characteristics with *M. catarrhalis.*

The results of the above observations can be summarized in the statement that the mouse, inoculated with the sputum of a patient suffering from influenza, died of a septicæmia due to the presence in the blood of: *Pneumococcus* Type 2, Rockefeller; *B. influenzæ*, strain Bassett-Smith 4; *M. catarrhalis.* The above findings were sufficiently interesting to ascertain if this recently isolated strain of *B. influenzæ* could of itself produce a demonstrable septicæmia in mice. In order to study this question, three series of mice were inoculated intra-peritoneally.

First Series.—The inoculum consisted of Pneumococcus Type 2 together with the freshly-isolated *B. influenzæ.*

Second Series.—The *B. influenzæ* alone.

Third Series.—*B. influenzæ* (Bassett-Smith strain) together with Pneumococcus Type 2.

All the above died within twenty-four hours of injection. They were carefully examined post mortem. Blood films were prepared from each and suitably stained. The heart-blood in each case was aseptically pipetted off and smeared on blood agar plates and cultured in blood broth. The lungs were preserved for histological examination.

The First and Third Series.—The *pneumococcus* was re-isolated in each case from the cultures from the heart-blood, but not the *B. influenzæ*. The tissues showed the usual morbid changes associated with pneumococcal septicæmia in mice. The spleens were notably enlarged.

The Second Series, that is, the mice inoculated with *B. influenzæ* alone, were found on examination to have died from a *B. influenzæ* septicæmia. The cultures from the heart-blood yielded a Gram-negative bacillus similar in every respect to the original strain employed.

This re-isolated *B. influenzæ* (patient's organism) again agglutinated to a titre of 1 in 191 with the Bassett-Smith type serum. Morphologically, it showed a tendency, when subcultured frequently, to be somewhat longer and to exhibit more filamentous forms than the bacilli of the primary cultures.

The post-mortem examination of these mice revealed an adherent pericardium and congested lungs, which were much softened and had a hæmorrhagic appearance. The spleens were of normal size. Histological examination of the lungs showed marked congestion of the blood-vessels with leucocytic emigration. The air vesicles contained in some places large patches of extravasated red blood corpuscles.

The points of interest in the above investigation are: (*a*) The isolation, following subcutaneous inoculation of sputum, from the heart-blood of a mouse, of three organisms which are so commonly associated in the clinical syndrome recognized as influenza; (*b*) the occurrence of a demonstrable septicæmia due to *B. influenzæ*; (*c*) the comparability of the pathological changes in the lungs of a mouse dying of influenzal septicæmia, experimentally produced, to those observed in the human subject in fatal cases of influenza.

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NOTES ON THE INFLUENZA EPIDEMIC, WITH SPECIAL REFERENCE TO PNEUMONIA IN MACEDONIA.[1]

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In a note on epidemics published in June, I pointed out some peculiar aspects of the epidemic in its inception. Since then unexpected opportunities of studying the epidemic in different centres have presented themselves. The observations arising therefrom are such that it seems to me to justify elaboration of these earlier remarks and placing one's findings on record whilst the picture is vivid.

It is difficult at the moment to place the epidemic in proper perspective, and indeed the picture is as yet incomplete, for though the acute stage is now over we are faced with the possibility of sequelæ for some time to come. Some of these are even now obvious and more especially those due to disintegrative or non-reparative changes in the lungs—some severe and presenting no difficulties in interpretation, others milder and indefinite but likely to interfere more or less seriously with the life and work of the individual.

Material on which Observations are based.

This has been confined to soldiers. My movements have brought me by chance into districts at the time coinciding with the beginning of the epidemic.

In the spring in France the earliest cases of a mild type, which I have described as of a peculiar glandular type, were admitted in large numbers to the isolation wards under my care.

In June, whilst doing duty at the Royal Herbert Hospital one noted at the beginning of the epidemic in that area numerous cases of a more severe and mixed, though not fatal type.

In September, whilst in charge of the Medical Division of the 63rd General Hospital in Salonika, the wards were filled with cases in all grades of severity and many fatal. And moving with the Army of Occupation to the Dardanelles in December a fresh and severe outbreak came under observation in a number of Anzacs who had come from the Jordan Valley where there was a shade temperature of 120° F., to meet adverse conditions of transport and climate on a bleak and exposed spot on the Peninsula. With these must be included a sprinkling of men who had come in January under similar circumstances from Bangalore, though, these stopping at Salonika, *en route*, had left the majority of their severe cases in hospital there. It is possible that these acquired the infection whilst in a depot at

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Salonika. Some officers who had been taken prisoners at Kut and confined in Asia Minor until the Armistice had detailed in their diaries an account of an epidemic amongst the inhabitants and themselves in a village of Yosghad which began on October 4.

To offer statistics would only be misleading. The physique and previous health of the men varied in different districts. In Salonika the men were often much debilitated and furthermore the outbreak coincided with the season of malaria which confused the diagnosis in many cases. Here the mortality was great and out of 100 consecutive pneumonias, fifty died.

In the Dardanelles, out of about 900 Anzacs, over 150 were admitted with influenza; of these 25 developed pneumonia and 12 died.

Exceptional opportunities for observation present themselves in a general military hospital, and especially in Macedonia where evacuation was necessarily slow—and patients were kept till convalescence was advanced. In some cases the disease actually developed in patients convalescent from other diseases. At the same time one must deplore many lost opportunities for research owing to the exigencies of the Service. Indeed, at the Dardanelles, in the absence of a pathological laboratory, it was necessary to carry on the work with the aid of a small travelling microscope and some stains acquired from a hospital ship and the local Turkish hospital.

Path of Infections.

It would seem that infection is carried by human traffic, judging from the times at which the epidemic originated at different parts of the world. The leave trains from Salonika were responsible for much, and cases often fatal were evacuated *en route*. Amongst the Anzacs the disease broke out on a crowded transport on which they were detained for several days before disembarking. But it is difficult to account for the outbreak in the middle of Asia Minor—120 miles east of Angora—unless, as was suggested, it had been brought from the Black Sea. There can be little doubt that overcrowding and poor ventilation are potent factors in the spread, and such are difficult to avoid in transports and troop trains.

Manifestations. (1) *Clinical.*—The condition is essentially a toxæmia which exerts its activity primarily and principally on the respiratory system and to a much lesser degree and much less frequently on the gastro-intestinal tract, and occasionally on the nervous system.

The milder cases present a striking similarity of symptoms—sudden onset with malaise and pains in head, back and limbs, pyrexia and intense congestion of pharynx and upper air passages without any increase in pulse rate, and terminating in two or three days by crisis or brief lysis.

Increasing grades of severity are associated with more extensive involvement of the respiratory tract from above downwards. In the most serious cases there is general affection of the lungs and a most fatal type of pneumonia in which the toxæmic symptoms are complicated by a characteristic manifestation of pulmonary obstruction.

In all cases, however, the respiratory tubes and tubules are first affected, and it is on the mucosa that the toxin particularly acts. Hence it is possible to pick out from a series of cases types in order of severity though often the types blend. Clinically we find (1) pharyngitis with or without implication of the mucosa of the nose and sinuses; (2) laryngitis; (3) tracheitis; (4) bronchitis; (5) bronchiolitis; and (6) pneumonia with involvement of all the lung tissues.

In any case the disease may terminate by crisis or rapid lysis as in the mild type after a few days. Occasionally there may be hoarseness or loss of voice for some time after the larynx has been affected, and some debility. But in the earlier cases seen in France this was not a noticeable feature. The men were returned to convalescent camp in a few days.

Further points concerning the milder cases are indicated in the charts appended, and it is not proposed to deal further with them here, save in one particular. The associated adenitis which was so marked a feature in the earlier cases as to suggest a diagnosis of German measles was not so marked in the later cases; though not infrequently cases exhibited many hard enlarged glands in the cervical, axillary, and even inguinal regions. The significance of this will be discussed later.

The Pulmonary Type.

The manifestations of this type are so varied in their clinical detail that it is difficult to give a general description. But it can be said that in the main the symptoms fall into two groups: (1) toxæmia; (2) mechanical, though the more or less asphyxial state produced thereby presents symptoms closely resembling some due to the toxæmia. Again, the picture varies in different outbreaks. Sometimes the toxæmic symptoms predominate, producing a drowsy and lethargic state with indefinite physical signs of pulmonary disease. At others the obstructive lesions are more manifest with coughing, cyanosis, asphyxia and noisy patients. This variation in type has been noted frequently. In Salonika there was a period when the incessant and for the most part unproductive coughing made the night a veritable and painful din. But in the Dardanelles there was throughout an ominous quiet in the wards. In the diary of the Kut officers is noted that the roaring and barking of the gasping dusky patients could be heard far from the huts.

The physical signs of involvement of the lungs are often most misleading at the outset, and even when in a few days definite evidence of consolidation of one or more lobes is manifest, it still must be appreciated that the entire lung tissue is in all probability affected. A central pneumonia may gradually reach the surface and present signs of consolidation.

A case may simulate middle ear disease or cerebral disease for the first few days.

Physical signs must be interpreted in the light of general symptoms

and with care ; indeed, it must be said that the physical signs of pulmonary involvement are of lesser importance than the objective signs and general condition of the patient.

Symptoms in Detail.—The recumbent position is usual and only rarely is there any desire to sit up. Indeed, this is the only position of comfort, and attempts to sit the patient up for examination may only lead to paroxysms of coughing. Some are particularly tranquil throughout and cheery, others have a sense of impending death, which is nearly always justified.

Cyanosis is a frequent and marked feature. It is apparently in direct relation to the extent of the pulmonary mischief, and, indeed, is often a better index of this than the physical signs themselves. It is furthermore of great prognostic value. In the early stages, and often during the long convalescence, it is of a lighter hue, the cheeks may be flushed whilst the ears are deeply cyanosed ; later it becomes more intense and universal, and in the still later stages produces a dusky black complexion—a condition that suggested to one medical officer the name of the "black death."

It is evidently symptomatic of an asphyxial state and not connected with the toxæmic. It is only found in connexion with pulmonary involvement and varies directly with this. It is increased by the most trivial exertion, such as coughing or drinking, or even talking, and in the convalescent can be excited by exertion. Though of grave significance, deeply cyanosed cases can and do recover often after many weeks. In some stages it produces the impression that the lungs are working to the limit of their reserve power, and in convalescence it must be regarded as an index of lung damage and to restrain unnecessary exertion. Attempts to relieve cyanosis by venesection have failed, and, indeed, the evidence is against it being of cardiac origin.

In a few cases, however, cyanosis occurred in association with distended cervical veins and appearances of cardiac dilation ; these were occasionally relieved by venesection.

The blood in severe cases is black, and sometimes even tarry. In the most extreme cases the patient died with asphyxia and severe agonal convulsions ; he was black in colour and the pulse remained good to the end.

Respiratory Distress.—The respirations are increased out of proportion to the pulse-rate, which, in fact, may remain normal. A rate of 40 per minute is common, and in some even 60 ; and in one it persisted at 90 for a day before death. In the early stages it assumes an emphysematous type, the expirations being prolonged, and with increasing severity of symptoms the expirations become longer and longer in comparison with inspirations, or else there may be gasping and quick panting, with hardly any movement of the chest-wall, into which, indeed, little air enters ; or in other cases the breathing may be noisy and roaring in character, as if purely tracheal in origin. In many cases there is actual distress with or without exertion.

It is important to note that (1) it is only in the pulmonary type of disease that these respiratory variations occur. (2) Venesection fails to give any relief; and (3) histological examination shows sufficient destruction of aerating tissue to account for the symptoms; and (4) the condition is often relieved, though only temporarily, by administration, preferably continuous, of oxygen. (5) Alteration in position of the patient produces no improvement.

The respiratory changes must then be regarded as indicative of pulmonary mischief, and as such are of prognostic import. Of grave moment is the combination of intense cyanosis and rapid breathing.

The Pulse.—The pulse-rate, as in milder cases, may in the pneumonic type be slow, but often is raised to 100 and sometimes more, but not in proportion to the respiratory increase. Only rarely is there dilation of the heart, and in grave cases the pulse-rate may be over 120. Death does not occur from cardiac failure, and in one series of cases at autopsy the myocardium was firm, though in the Anzac series there was distinct evidence of myocardial degeneration. In some cases, indeed, the pulse was good until the end, and in one it was even felt for a brief period after respirations had ceased.

Other Symptoms.—Occasionally cerebral symptoms are seen. Sometimes delirium is an early symptom, in others a late one. Lethargy is characteristic of the toxæmia. Deafness may arise early, and sometimes indefinite signs of mastoid disease. Vomiting is frequently met with accompanied by furred tongue at the outset of the illness and diarrhœa occasionally. Albuminuria of slight degree often accompanied the febrile disturbance.

Hæmorrhages are not uncommon. Epistaxis may occur in the early stages. With the cough there may be pinkish (blood-stained) sputum; rarely is the typical rusty sputum seen. Occasionally the sputum contains dark-coloured blood and clots for a time, and sometimes more extensive hæmorrhage results with bright red blood at the onset. The intense engorgement of the mucous membranes and the pulmonary capillaries and also the definite infarction sometimes seen will account for these symptoms.

Physical Signs.—These are very anomalous, and vary even in the same patient from time to time. They appear to be the result of obstruction to the bronchioles with more or less surrounding consolidation intermingled with areas of emphysema. The signs vary with the accumulation or evacuation of the secretion of the bronchioles, so that at one moment the lung may be silent and at another may present signs of consolidation.

The most characteristic and frequent finding is a fine crepitation heard over a considerable area, often more marked on deep respiration or after coughing. Sometimes the signs are slight, and suggest a central pneumonia with relaxed or emphysematous lung surrounding, and in a few days the consolidation reaches the surface with characteristic signs. But only occasionally are there definite classical signs of lobar consolidation; usually the mixture of lobular consolidation and emphysema produce indefinite

signs. Hence one finds varying signs as follows: (1) Crepitations; crepitations with absolute dullness. (2) Crepitations with impaired percussion note. (3) Crepitations with whispering pectoriloquy with or without tubular breathing. (4) Silent lung. (5) Choked lung into which little air enters with great difficulty, relieved sometimes on coughing; with resolution the sounds become coarser and râles appear. It may be taken that generally signs of choking of lungs or even spreading consolidation will be found posteriorly and latterally, whilst anteriorly there is evidence of emphysema in a hyper-resonant lung with harsh breathing. The middle lobe is frequently implicated with the lower lobe. Occasionally, but rarely, the upper lobe on one side is consolidated with or without similar lesions in the lower lobe.

Sometimes signs of spreading pneumonitis (for this is, perhaps, a better term than the more specific designation of pneumonia) are noted, and the lesion beginning at the base may implicate in time the greater part of both lungs; at times one part may show resolution, whilst another becomes affected as in pneumonia migrans. But always, as has been pointed out above, the signs of localized consolidation are misleading, inasmuch as the entire lung tissue is probably affected. Occasionally but rarely pleural effusion occurs even with whispering pectoriloquy and tubular breathing in connection with absolute dullness—a condition verified by exploratory puncture.

Significance of Physical Signs.—There is little relation between the signs enumerated above and the severity of the disease. A fatal case may present crepitations throughout a brief illness. But, perhaps, a definite and early appearance of lobar consolidation may be more hopeful than signs of diffuse lesions. Here it is important to note that the signs of lobar consolidation do not necessarily imply lobar pneumonia. Clinically then occurs bronchitis, pneumonitis, broncho-pneumonia, massive consolidation, effusion, and emphysema.

Sputum.—The sputum and the cough are very variable. Usually there is little in the early stages, sometimes blood-stained and pinkish, rarely rusty, sometimes actually containing blood. There may be no cough or a dry cough, or at times paroxysms of barking, with little expectoration, which often is only brought up with difficulty. In the later stages the cough weakens and the act is painful. Often the cough throughout is insignificant. In some there results large quantities of highly albuminous glairy fluid with whitish muco-purulent matter therein. With resolution the sputum changes to nummular type, but it is not profuse, and with breaking down lung tissue it becomes actually purulent. Quantities of purulent matter may be expectorated for several weeks in cases which die, showing evidence of suppuration and breaking down of large areas of lung tissue.

Progress.—In favourable cases the acute symptoms end by crisis in some, by lysis in most. But though it would seem that the toxæmia has been overcome, the pulmonary lesions do not immediately resolve. Indeed

resolution may be prolonged for weeks, and is always slow. Consequently, even when the temperature falls by crisis, the respirations remain increased, and only regain their normal rate with improvement in the pulmonary state. Similarly cyanosis may persist for a long time, and be accentuated by slight exertions; hence a long convalescence is indicated.

The silent and unresolved lung may persist for weeks and perhaps indefinitely. But the future state of the unresolved lung remains to be followed out. The affected side may be dull and the signs simulate fluid. In these cases a pyrexial curve is sometimes obtained, in some slight, with rise of 1° or 2°, in others more marked. In one case the rise was only noted at 6 a.m. each day.

Where there is actually pleural effusion a serous highly albuminous fluid may be evacuated and occasionally thick purolymph.

The unresolved lung may undergo further changes, either reparative with appearances of crepitations and moist sounds accompanied by a disappearance of the radiographic shadow; or disintegrative with abscess formation. Signs of cavitation with purulent expectoration and hectic temperature may herald a fatal result. Or organization may lead to healing and recovery after a long convalescence. In this connexion it is feasible to anticipate conditions of bronchiectasis and chronic interstitial fibrosis arising in the unresolved lung, but this remains to be seen.

The voice when lost often does not return for weeks and occasionally there is actual ulceration of the cords.

In the fatal cases, from which alone one can surmise the processes of events in those that recover, the processes are all more intense. Death may occur from acute œdema of the lungs at the beginning of the illness, associated with respiratory distress, cyanosis and much frothy (in some cases blood-stained) fluid welling up and pouring from the lips and nostrils; the patient actually dying from drowning. In others there is more obstruction and asphyxia with little expectoration, but the complexion becomes dusky, purple or black, and agonal convulsions accompany death.

Again there may be more evidence of resistance and reaction on the part of the patient, but the lesion attempting to clear from one part spreads to another. Here a surprising respiratory compensation is manifest, for with only a portion of lung tissue still aërating life is often maintained for days notwithstanding that the acting lung tissue is itself highly emphysematous, so that respiration becomes more rapid, more laboured, the inspirations become gasps, the expirations drawn-out sighs, and ultimately death results from exhaustion. The deeply cyanosed state with gasping noisy respirations may persist for hours and even days, belying all prognosis of immediate death.

Pathological Findings.

These are significant of an acute irritation of the air passages with a responsive reaction on the part of the mucosa. There is intense engorgement of the capillaries and a pouring out of exudate into the lumina of the tubules and alveoli accompanied by softening of lung tissue and a vicarious emphysema of the less affected parts. The trachea was frequently deeply engorged and of a purplish tint and in a few cases there was definite ulceration of the vocal cords. In brief there occurs tracheitis, bronchiolitis, consolidation softening and emphysema.

The stress in the first place appears to fall on the tubules, but the lesions are far more extensive than the first glance at the autopsy would denote. For indeed there is actually a generalized bronchiolitis which is seen even in the emphysematous and more normal parts. In more advanced lesions there is peribronchitis with cell exudations, capillary engorgement and alveoli choked with serous fluid, and varying amounts of connective tissue and round cells with blood corpuscles in many; and in further advanced cases round cells and in some collections of polymorphonuclear cells as in grey hepatization. Consequently areas of consolidation are found either nodular and discrete or aggregated into pneumonia of lobar or massive distribution and the picture varies with the intensity and stage of the reaction. So that most frequently there appears on opening the chest voluminous bulging pale emphysematous lungs filling the thoracic cavity and purple consolidated œdematous implication of all the posterior and dependent parts, this spreading more or less laterally and often involving the whole of the middle lobe. Rarely the upper and middle lobe are most affected, or there is a diffuse nodular consolidation of all the lung tissue. In addition there may be hæmorrhagic areas or collapsed areas. In cases that die after a brief illness the consolidated process may not be evident but there is engorgement and intense œdema. But however varied may be the anatomical picture of broncho-pneumonia consolidation, two conditions have been found in every autopsy and these are perhaps the more important factors. Always there has been *universal friability* of lung tissue and *emphysema*. The lungs throughout, even in the parts apparently normal, have been soft and friable and gave way to the touch, often being of an almost butter-like consistence. This change is in no wise a post-mortem one, for often the autopsy was done immediately after death. The emphysema is both macroscopic and microscopic. In the anterior and uppermost parts it is often very marked and in a few cases large bullæ have been found associated with the upper lobes and anterior border. Histologically these areas show the fusion of alveolar walls usual in emphysematous lung of long standing. But even in the consolidated parts one finds microscopic areas of similar emphysematous nature.

It is to the two conditions that especial attention must be directed and the other changes can be considered of lesser importance. The pleura is not often affected, occasionally it was dulled and injected over more

consolidated areas, rarely there was pus and occasionally fluid. Not infrequently sub-pleural petechiæ (Jardieu's spots) in large numbers pointed to the asphyxial state.

The glands in the bifurcation of the trachea were in nearly all cases much enlarged and deeply engorged, and in some even breaking down and diffluent to a lesser degree. The glands along the trachea and main bronchi were similarly affected and occasionally the glands in the posterior triangle of the neck and the axilla. Histologically the bifurcation glands showed enormously engorged capillaries with proliferation of endothelial cells and evidence of great activity.

The heart showed varying changes. In a large number of cases the muscle was firm and there was no naked-eye change, but in others and in all the cases amongst the Anzacs the muscle was soft and friable and there was histological evidence of degeneration. In many the cavities were filled with pale agonal and post-mortem coagula, but dilatation was not noted. In a few cases of intense asphyxia the cavities, especially the right side, contained much blackish coagulum. In two cases there was infective endocarditis with large pendulous vegetations on the aortic cusps and inflammation of the myocardium at the base of these.

The remaining viscera showed the usual febrile changes, though in many cases there was varying enlargement of the spleen due to malaria and in these the parasite had been found either in life or in smears of spleen at post mortem.

Discussion of Findings.

It is evident that the specific changes occur in the lungs and that the entire lung tissue is implicated. But the nature of the lesions is open to discussion. Is there a destructive activity exerted by the toxin on the lung tissue in the first place which facilitates the emphysematous change; or is the emphysematous change associated with so much destruction of elastic tissue as to produce of itself an undue friability?

These points have yet to be worked out and in connexion with them one might recall here those cases of acute bronchiolectasis (with blistered lungs) occurring occasionally in children dying with bronchopneumonia.

Again is the friability a condition compatible with recovery, or is it invariably associated with fatal cases alone? This is impossible to prove by direct evidence, and the same line of thought has been applied to the condition of hepatization of the lungs in true croupous pneumonia. It would indeed seem impossible to expect resolution in so friable and emphysematous a lung as one meets with in the post-mortem room. But later investigation of cases in the light of these suggestions incline one to the belief that no case is hopeless until dead and the recuperative power is indeed remarkable.

But whatever may be the interpretation of these anatomical findings, there can be no doubt that the lungs are extensively damaged, and clinical evidence alone points to the permanency of the damage. This is the

important factor to bear in mind in dealing with the many convalescent cases from the epidemic. It has been pointed out that the cyanosis persists for long after recovery and exertion increases this; many also complain of indefinite pains in the chest. Again we must add that time alone will settle many of these points.

Reactionary Manifestations.

(1) *Specific.*—To determine the proper line of treatment it is necessary to appreciate the natural reaction of the system in those cases which recover as well as the nature and action of the causal agent.

Notwithstanding that, after the failure to isolate the Pfeiffer's bacillus in earlier cases, many observers have found it in the majority of cases examined, there is still some uncertainty as to its being the sole causal agent. Nevertheless it is evident that we are dealing with a toxæmia of great and rapidly acting virulence which exerts its activity on the respiratory tract. That it is not a septicæmia is evident; blood cultures for the most part have been sterile; some animal inoculations into rabbits with the blood of grave cases produced no general infection, indeed there is no evidence that the bacteria exist in the blood-stream. It is obvious also that the toxæmia can be successfully resisted by the patient who recovers. An understanding of the processes at work must determine specific treatment.

Blood Changes.—There is no inflammatory response as seen in lobar pneumonia. On the contrary in influenza alone a leucopenia is the rule, though during prolonged resolution and more especially in abscess formation there is an increase of the polymorphonuclear cells. In the sputum also the pus cell is not a marked feature in uncomplicated cases, nor is there any degree of cell exudation comparable with that in grey hepatization.

The changes noted are: (1) A relative lymphocytosis; (2) activity of adenoid tissue. The significance of this lymphatic activity is not obvious at present. But, as previously described, there is often a polyadenitis and, in later phases of the epidemic where cervical adenitis was marked, prognosis seemed better. In the post-mortem room marked changes have been noted in the mediastinal glands but it has yet to be shown whether Pfeiffer's bacilli are present in the glands. It is probable that this lymphatic activity plays a great part in the reaction to infection.

The intense capillary engorgement and exudation of a highly albuminous serum must also be concerned in the reactionary process. And general observation suggests an elaboration of an antitoxin in the patient's blood. We have slight clinical evidence in one case in which treatment was based on this supposition.

(2) *Reparative Reactivity.*—The questions of the damaged lung and the possibility of repair of the friable and emphysematous lung, etc., have been dealt with above. On the hypothesis then that the condition is one of

toxæmia, which leads to production of antitoxin and yet causes a certain degree of anatomical change, our treatment must be based.

Causes of Death.—These are (1) œdema, (2) asphyxia, (3) exhaustion, and (4) rarely, cardiac failure. For the most part death comes from failure of the respiratory system.

Treatment.—A survey of the track of the epidemic demonstrates that we are dealing with a mass infection which is spread along the lines of and by human traffic. The question whether this can be controlled is too big to touch on in these notes and it is highly improbable that prophylaxis could ever be complete and especially in war time. But much could be done to alleviate such conditions as overcrowding in huts, barracks and offices, and of great import in the light of demobilization, the condition of life in transports and troop trains. Also the movement of troops to adverse climatic conditions and unsuitable depots and rest camps. Local centres can do much to diminish the incidence by suitable ventilation, etc.

Individual Treatment.—This at the moment is purely symptomatic and, though many specific remedies have been advocated none has proved satisfactory. The general management of the patient determines much and can be summed up as follows: fresh air, rest, sustenance and nursing. At 63rd General Hospital our pneumonia cases were collected into five marquees each containing fourteen beds, and the sides removed day and night, protection being only afforded when necessary from the occasional bleak winds. This was practically open-air treatment. The diet was suited to the patient's fancy and no restrictions were made. Brandy, six ounces or more in the day according to previous habits, and champagne were freely given, and in convalescence port wine.

Medicinal treatment was of little avail. Salicylates certainly relieved the pains in the toxæmic stage. Expectorants were useless and later discarded. Inhalations, menthol and eucalyptus, gave much relief.

Morphia and, where obtainable, heroin were used at all times to produce sleep, Dover's powders repeatedly at night time, and there can be no doubt as to their benefit from the rest obtained and in no case was there any evidence of a harmful influence. The most serious cases demanded sleep and were never refused it, and with convalescence morphia was stopped. This unconventional use of morphia, as was expected, aroused some anxiety on the part of one's more timid colleagues, but, notwithstanding the theoretical dangers, the rest resulting from its use could only have been productive of good. So, after putting the matter before the consulting physician, we no longer spared the drug.

Camphor was given in small and large doses with no appreciable result.

Atropine was used freely in cases of marked œdema but was soon discarded.

Digitalis and strychnine were used to a great extent at first, especially with a rapid pulse, and continued in smaller doses later, but no appreciable effect could be noted.

Cyanosis was relieved by oxygen in many cases. At first venesection was tried but without any success, except in those rare cases presenting signs of cardiac dilation.

Quinine was given in large doses, often intravenously, in cases complicated by malaria and in delirious cases mistaken for cerebral malaria but no effect either good or bad could be determined.

After a time poulticing was introduced with the aid of linseed and used extensively, most of the patients were considerably relieved thereby and it seemed that much good resulted. After this as a routine treatment all cases on admission were given Dover's powder, grains 15, and as soon as signs of pulmonary involvement were manifest linseed poultices were applied.

Relation of Malaria to the Disease.

In Macedonia there was always the possibility of malaria to be considered both from the point of view of diagnosis and treatment. The presence of malaria was determined, often by hæmatological examinations but more often at autopsy by pigmentary and splenic changes.

Some of these cases recovered, but for the most part the combination of malaria and pneumonia was a very fatal one.

At first the cerebral symptoms of influenza were mistaken for those of cerebral malaria and treated accordingly. Also there was some hesitation as to administration of quinine in view of its effect on the reactionary processes. But later all suspected cases were given quinine as stated.

Specific Treatment.—On deliberating over the less acute cases which lingered for days or weeks and presenting signs of spreading involvement of the lung tissue, it seemed that the primary infection was complicated by secondary infections suggestively of pyogenic nature. Hence one naturally turned to vaccines for assistance. Two vaccines were employed. In the first I punctured a lung immediately after death and obtained a pure culture of a minute coccus, nature undetermined, and from this the vaccine was made. The other was supplied from the central laboratory and was a mixture of streptococci. Series of cases were taken, and, though it seemed at first that satisfactory results ensued, it was obvious that identical results obtained in the control series.

With the growing conviction that the essential process was one of toxæmia, attention was directed to serum-therapy and we had in mind the idea that in the blood of convalescent patients would be found the antitoxin itself, and we are still of this opinion. Unfortunately various difficulties pesented themselves and it was not until the end of the epidemic on the Dardanelles that we found an opportunity to put these ideas into practice and then in only one case.

The patient was gravely ill, and indeed we had seen no other case of such gravity ever recover. But he was given serum from several picked